# Review of Vinyl Graft Copolymerization Featuring Recent Advances toward Controlled Radical-Based Reactions and Illustrated with Chitin/Chitosan Trunk Polymers

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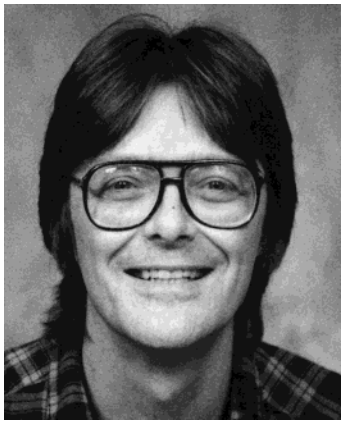

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## *I. Introduction*

### A. Definition and Potential Applications of Graft Copolymers

In addition to other complex polymer systems comprised of star, block, and dendritic architectures, graft copolymer synthesis is an important aspect of polymer science which continues to receive considerable attention.[1] Graft copolymers can be described as having the general structure **1**, where the main polymer backbone A, commonly referred to as the

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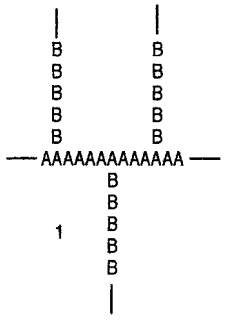
trunk polymer, has branches of polymer chain B emanating from different points along its length. The




common nomenclature used to describe structure **1**, where polymer A is grafted with polymer B, is A-*graft*-B, which can be further abbreviated as A-*g*-B. Graft copolymers have a variety of potential applications resulting from the wide range of properties available when different polymer chains are connected to form a hybrid branched macromolecule.

Much research has been conducted on the use of high-energy $\gamma$-radiation for the synthesis of grafted derivatives.[2] When polymeric materials are exposed to $\gamma$-radiation, radicals, cations, and free electrons can be generated, and it is the formation of free radicals on the polymer backbone that facilitates the formation of grafted chains. The radical formation upon exposure to the radiation is an extremely convenient technique from the viewpoint that no "synthetic steps" are necessary; all the reagents needed are the polymer to be grafted, the monomer, and solvent (if necessary). With this versatility, many different grafted derivatives have been synthesized for potential use in several interesting applications. Cross-linked poly(ethylene oxide), having heat-shrinkable properties, can be used as a sutureless method for connecting blood vessels. Biocompatibility is an ever present issue with biomaterials;[3] improvements in the biocompatibility of this material were observed by radiation-induced grafting of styrene, butadiene, and ethylene from the cross-linked poly(ethylene oxide) substrate.[4] For applications such as artificial heart valves, silicon rubber grafted with *N*-vinyl pyrrolidone and natural rubber grafted with 2-(*N*,*N*-dimethylaminoethyl) acrylate (both synthesized with radiation techniques) appear to be useful biocompatible materials; however, the latter derivative's biocompatibility is higher than the former.[5−7] Graft copolymerization has several important applications in the textile industry. For instance, improved soil release and fabric comfort can be obtained from grafting fibers with hydrophilic monomers. Moisture absorbency of cellulose fibers was greatly increased (as high as 3000% water uptake) by radiation-induced grafting of acrylic acid from the fiber followed by cellulose decrystallization upon exposure to $ZnCl_2$.[8,9] Grafting a fabric's surface with the appropriate monomer can improve abrasion resistance. For example, the growth of poly(ethyl acrylate) chains from cotton fabric by means of exposure to $\gamma$-radiation showed improved resistance to abrasion.[10] Flame retardency of fabrics is an important safety concern in many aspects of textile end uses. Due to the flame resistance of halogenated and phosphorus-based materials, radiation-induced grafting of vinyl bromide and different vinyl phosphonates from polyester and polyester/cotton-blended fabrics resulted in much improved flame retardency.[11−13]

Due to their influence over interfacial adhesion and friction,[14] graft copolymers have tremendous potential for improving the mechanical properties of composites. Since polymers of different chemical structure do not generally form intimate mixtures when blended together, the interfaces between dissimilar polymers (polyA and polyB) in a composite requires some type of adhesive for high-strength applications. Graft copolymers are ideal for this type of situation. When a hybrid branched macromolecule (polyA-*g*-polyB) is placed at the interface between polyA and polyB, the respective portions of the graft copolymer diffuse into the bulk portion of polyA and polyB. Although an overall bulk phase separation between polyA and polyB remains, the graft copolymer positioned at the interface provides a stronger bond between these two phases. Incorporating small amounts of poly(ethyl acrylate) (PEA)-*g*-poly(styrene) (PSt) into PEA/PSt blends increased compatibilization and results in tensile strength increases due to increased interfacial adhesion between PEA and PSt phases.[15] Commercial elastomers such as butyl rubber, poly(isobutylene-*co*-isoprene), have useful properties, such as low air permeability, but suffer however from a lack of compatibility with other polymeric materials. Grafting methyl methacrylate side chains onto butyl rubber trunk polymer has been performed in an attempt to improve interfacial compatibility for possible use with other elastomers and plastics.[16] Generating composites of wood and polystyrene bonded with phenol formaldehyde resin still requires a compatibilizing agent in order to further bond these two dissimilar materials together. Narayan et al. observed that the placement of various cellulose-*g*-polystyrene derivatives at the wood/polystyrene interface in the presence of the phenol formaldehyde resin improved the shear strengths of the layered materials.[17]

An interesting medical application for graft copolymers, where reductions in frictional forces between two dissimilar surfaces are desired, is in the area of tubular devices (catheters and cytoscopes) which are, as necessary for examination, inserted into various bodily orifices.[18] For example, the surface grafting of a poly(urethane) film with dimethyl acrylamide resulted in a decrease of the coefficient of friction when the substrate was in the fully hydrated state.[19] Glass-ionomer cements (GIC) have received attention for dental applications due to such properties as fluoride release, thermal compatibility, and biocompatibility. However, the current low strength and brittleness of this material makes practical use difficult. Improvements in this area have been made using light-curable *N*-vinylpyrrolidone grafting of GIC, which showed improvement in both flexural and compressive strengths.[20] Grafting poly(dimethyl siloxane) with styrene using an atom transfer radical polymerization (ATRP) mechanism, to be discussed in later sections, was performed to yield derivatives

with potential applications such as supercritical $CO_2$ surfactants and thermoplastic elastomers.[21]

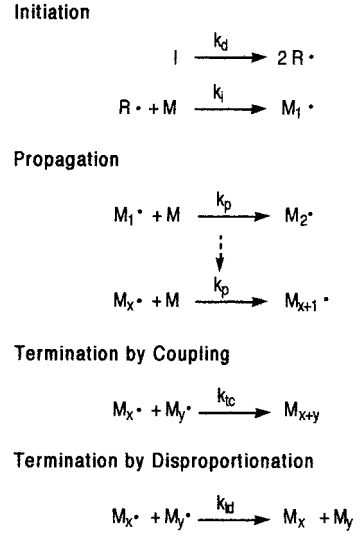
Several examples have been provided above to illustrate the impact graft copolymers can have on improving the properties of various end-use materials. Future applications of graft copolymers require an understanding of both intramolecular and intermolecular characteristics. These structure−property relationships are difficult to obtain without the ability to synthesize and characterize graft copolymers systematically. Besides having good control over the grafted chain molecular weight, the major problem encountered in graft copolymerization (especially with free radical-based systems) is the simultaneous formation of homopolymer. Homopolymer is essentially unattached polymer having the same chemical structure as that of the grafted chains grown from the trunk polymer. The major sources of homopolymer result from syntheses which lack specific macroradical formation and from the chain transfer of growing grafted chain ends. Not only is homopolymer a waste of monomer, but the separation of it from the grafted derivative is often difficult, and it thus creates problems in characterizing the graft derivative. *In fact, homopolymer formation is the major reason for the lack of a widespread industrial development of graft copolymers.*[22]

## B. Scope and Organization of This Article

Radical chain growth mechanisms are important to polymer synthesis due to their greater versatility, relative to cationic and anionic methods, in regard to the wider range of vinyl monomers that are polymerizable by this method. The overall focus of this article is to discuss various free radical polymerization techniques which have the potential to conduct radical-based graft copolymerizations of any trunk polymer utilizing a "grafting from" mechanism in a more controlled manner with minimal homopolymerization. A substantial portion of the article discusses different techniques, mostly free radical based, which have been used to graft chitin and chitosan trunk polymers. Chitin and chitosan are under-utilized renewable polysaccharides, and these grafting efforts have been performed with the intent of expanding the future applications of these biopolymers. Discussing chitin and chitosan grafting will provide a set of examples to illustrate the levels of homopolymer that can be encountered in free radical graft copolymerization. The remainder of the article outlines the mechanistic source of homopolymer and alternative radical polymerization techniques which have the potential to significantly reduce homopolymer formation while also promoting better control over the grafted chain architecture.

The article is organized as follows. Section II briefly reviews the kinetics of vinyl polymerization, in regard to initiation, propagation, termination, and chain transfer, and outlines the basic mechanism involved in a radical-based "grafting from" copolymerization. This provides a perspective for sections IV−VI. Section III provides general background information on chitin and chitosan, while section IV reviews the different techniques which have been used to graft these biopolymers and includes typical grafting and homopolymer yields. Section V critiques the free radical grafting methods for chitin/chitosan derivatization after discussing mechanistically what is necessary for grafting any trunk polymer in a controlled manner with minimal homopolymerization. Section VI describes how radical formation with redox techniques can strategically be used for specific macroradical formation and subsequently discusses various radical-generating redox methods. After realizing the limitations of the redox chemistries due to their conventional free radical character, section VII describes different controlled/"living" radical polymerization techniques and their possibilities in grafting synthesis, especially with regard to controlling grafted chain molecular weights with possible chain transfer minimization. Section VIII provides an article summary including remarks concerning the future use of these chemistries.

**Scheme 1. Reaction Mechanism for the Classic Radical Polymerization of Vinyl Monomer, M, Initiated by Homolytic Dissociation of Species I**




## II. Conventional Free Radical Polymerization

## A. Kinetics of Vinyl Polymerization[23,24]

The general mechanism for free radical vinyl polymerization utilizing an initiator that creates radicals by homolytic dissociation can be represented by Scheme 1. The kinetic rate laws for initiation ($R_i$) and termination ($R_t$) can be described by eqs 1 and 2, respectively

$$R_i = 2fk_d[I] \quad (1)$$

$$R_t = 2k_t[M^{\bullet}]^2 \quad (2)$$

where $f$ is the initiator efficiency, $k_t = k_{tc} + k_{td}$, and $M^{\bullet}$ is a propagating polymer chain end. Using the steady-state assumption where the radical concentration is assumed to be constant by setting $R_i$ equal

to $R_t$, the concentration of M$^\bullet$ can be removed from the rate law expression for propagation ($R_p$), allowing $R_p$ to be expressed as shown in eq 3.

$$R_p = k_p[M]\left(\frac{fk_d[I]}{k_t}\right)^{1/2} \quad (3)$$

The kinetic chain length, $\nu$, is defined as the average number of monomer units that are polymerized by each initiating radical and can be quantitatively described by eq 4, where the rate of polymerization is divided by either the rate of initiation or termination.

$$\nu = \frac{R_p}{R_i} = \frac{R_p}{R_t} \quad (4)$$

Qualitatively, if the only reactions that initiating and propagating radicals were allowed to undertake were the addition of monomer and termination by either disproportionation or coupling, the number average degree of polymerization should be associated with the kinetic chain length. For example, termination by disproportionation would yield average degrees of polymerization equal to $\nu$, whereas average degrees of polymerization equal to $2\nu$ would suggest termination by coupling. Experience from end group analysis indicates that the predominant mode of termination is that of coupling, with disproportionation being rather uncommon. It was observed that under certain conditions, free radical polymerizations could be conducted where termination by coupling was dominant; however, molecular weights observed were much lower than $2\nu$ while maintaining comparable monomer conversion as expected from the $R_p$. The notion of chain transfer was postulated, as shown in eq 5, from these results

$$M_y^\bullet + X{-}R' \xrightarrow{k_{tr,X-R'}} M_y{-}X + R'^\bullet \quad (5)$$

where $M_y^\bullet$ is a propagating polymer chain with a degree of polymerization equal to $y$ and X−R′ is some organic species (monomer, solvent, etc.) with X being a transferable group, typically a hydrogen or a halide. The rate of chain transfer ($R_{tr,X-R'}$) to X−R′ can be described as shown in eq 6.

$$R_{tr,X-R'} = k_{tr,X-R'}[M_y^\bullet][X{-}R'] \quad (6)$$

In the chain transfer reaction, the growth of the propagating chain is stopped by capping the chain end with the X moiety. However, the polymerization as a whole has not stopped if the new radical, $R'^\bullet$, is capable of initiating the growth of a new polymer chain.

To quantify the occurrence of chain transfer,[25] a relationship was developed as shown in eq 7, that equates the number average degree of polymerization ($\bar{X}_n$) to a modified form of the kinetic chain length expression (eq 4) where the rate of polymerization is divided by the summation of the rate expressions for all types of chain growth breaking reactions.

$$\bar{X}_n = \frac{R_p}{(R_t/2) + k_{tr,M}[M^\bullet][M] + k_{tr,S}[M^\bullet][S] + k_{tr,I}[M^\bullet][I]} \quad (7)$$

In the denominator, the terms ordered from left to right represent termination by coupling and chain transfer to monomer, solvent, and initiator. A quantity referred to as the chain transfer constant ($C_{X-R'}$) for an organic substrate, (X−R′) is defined as the ratio of the rate constant for chain transfer over the rate constant for propagation. This quantity measures the likelihood of transferring the radical from the propagating polymer chain to the particular organic substrate, X−R′. Chain transfer constants for monomer, solvent, and initiator can be represented as shown in eq 8, respectively.

$$C_M = \frac{k_{tr,M}}{k_p} \qquad C_S = \frac{k_{tr,S}}{k_p} \qquad C_I = \frac{k_{tr,I}}{k_p} \quad (8)$$

Making the appropriate substitutions with eqs 1, 2, 3, and 8, eq 7 can be manipulated to provide eq 9, commonly referred to as the "Mayo Equation".[25]

$$\frac{1}{\bar{X}_n} = \frac{k_t R_p}{k_p^2[M]^2} + C_M + C_S\frac{[S]}{[M]} + C_I\frac{k_t R_p^2}{k_p^2 f k_d[M]^3} \quad (9)$$

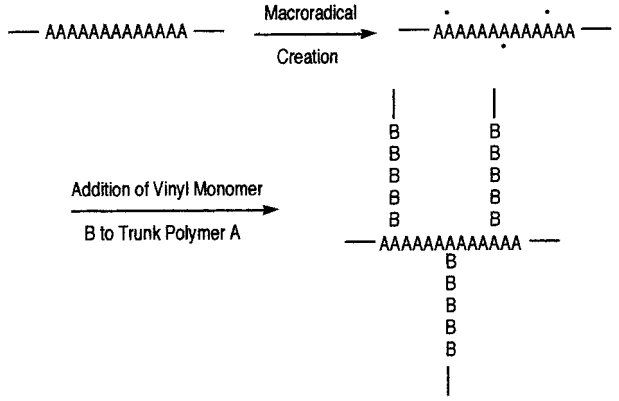
Chain transfer constants have been evaluated for a wide variety of compounds based on the relationship shown in eq 9, but the details of how they can be obtained are beyond the scope of this review.

## B. Graft Copolymerization Using a Radical Mechanism[26]

Vinyl graft copolymerization can be described as the modification of a preexisting polymer chain (trunk polymer) where polymer chains, comprised of different structural units from those of the trunk polymer, are grown from the trunk polymer backbone. The basic mechanism, as shown in Scheme 2, is commonly referred to as a "grafting from" mechanism ("grafting through" and "grafting onto" are described elsewhere[1]) and begins by creating free radical sites on the trunk polymer chain whereby vinyl monomer can react with the radical to propagate into a new polymer chain that is covalently bonded to the trunk polymer. This type of copolymerization offers the possibility of creating novel polymer systems that permanently combine the properties of both polymer chains.

Although it is not shown in Scheme 2, homopolymer, polymer B that is not chemically bonded to the

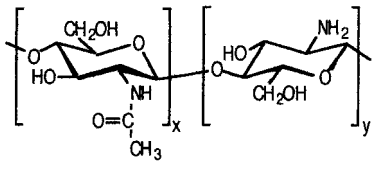
**Scheme 2. General Mechanism of Graft Copolymerization of Trunk Polymer A with Vinyl Monomer B by Means of a Free Radical Mechanism**




trunk polymer A, can be produced during the course of the reaction in several ways depending on the experimental conditions. Homopolymer can result if the initiator used is one that produces free radicals in solution (in the presence of vinyl monomer B initiating homopolymerization) before creating the trunk polymer radicals (macroradicals). Once a grafted chain has been initiated and begins to propagate, chain transfer from the growing grafted chain end can occur with some species in the medium to yield a free radical in solution that could initiate the growth of homopolymer B chains. These issues will be dealt with in more detail in subsequent sections which will initially concern grafting to chitin and chitosan.

## III. Chitin and Chitosan—Structure, Sources, and Uses[27−31]

Next to cellulose, chitin is considered to be the second most abundant natural organic resource on earth. Chitin can be found in marine invertebrates, fungi, insects, and yeasts. Depending on the source, it generally functions as an exoskeleton, providing structural integrity, commonly embedded in a matrix of proteins, minerals, and at times various other polysaccharides. Chitin is a homopolymer comprised of 2-acetamido-2-deoxy-$\beta$-D-glucopyranose units; however, some units exist in the deacetylated form as 2-amino-2-deoxy-$\beta$-D-glucopyranose. When chitin is deacetylated to at least 50%, it is referred to as chitosan and is soluble (depending on the molecular weight) in dilute acids existing as a cationic polyelectrolyte. Chitosan is essentially the N-deacetylated derivative of chitin. Chemical repeat structures of chitin **2** and chitosan **3** are provided below. Chitin




2 3

can naturally exist as microscopic crystalline fibrils in three different crystalline polymorphs, namely, $\alpha$, $\beta$, and $\gamma$, with $\alpha$ being the more common and most stable form. In terms of the polymer chain orientation, the $\alpha$ and $\gamma$ forms are believed to exist as antiparallel, stacked unit cells, with $\beta$ being comprised of parallel, stacked unit cells.

Chitin has not naturally been found in a highly purified form. Shells of marine crustaceans, mainly shrimp and crab, are currently the largest commercially available sources of chitin. On an industrial scale, chitin is typically retrieved by, first, an acid soak which is necessary for the demineralization of the shell. Next, the material is soaked in 20% (w/w) NaOH in order to breakdown the protein matrix. After a water wash and subsequent drying step, the remaining material is a purified chitin. Continuing the process further, chitin can be deacetylated to chitosan by heating chitin flake or powder at 120 °C under a nitrogen purge for 2 h in 50% (w/w) NaOH. This step needs to be repeated several times to achieve a high degree of deacetylation. Chitin can be converted to chitosan having a degree of deacetylation on the order of 95−98% with 3−4 deacetylation cycles; complete removal of *N*-acetyl groups is extremely difficult.

Since chitosan is soluble in dilute aqueous acids, it can be solution processed into a wide variety of physical forms. Chitin, being the more intractable derivative, is mainly used directly in the powder form. However, chitin can be regenerated from chitosan by selective N-acylation with acetic anhydride, and thus processing chitosan and chitin into films, fibers, shaped objects, beads, gels, and microcrystalline powders is possible. It is interesting to note that liquid crystalline suspensions of rodlike, chitin crystallites can be produced from acid hydrolysis of chitin flake.[32] The hydrolysis is conducted for a short time to mainly depolymerize the amorphous chitin, leaving the crystalline domains intact. At the proper concentration and pH, these suspensions can exhibit chiral nematic behavior that can be viewed as fingerprint textures under a polarizing optical light microscope.[33]

The high degree of functionality of chitin (two hydroxyl groups per repeat unit) and chitosan (two hydroxyl groups and one primary amine group per repeat unit) allows further derivatization with a wide range of compounds. Chitin and chitosan also exhibit biodegradable, antibacterial, and antifungal properties, making these materials attractive for a wide range of applications. Table 1 provides a collection of potential uses for chitin and chitosan that are categorized by physical form. In conjunction with utilizing the high degree of functionality of these polymers for the synthesis of new materials, several attempts have been made to permanently combine the properties of chitin and chitosan with those of synthetic polymers via graft copolymerization. Kurita reviewed the grafting of chitin and chitosan, providing detail on both the synthetic experimental conditions and the physical properties of the grafted derivatives.[34] Complimenting this information, the following sections will describe the mechanisms of various initiating methods used to synthesize a number of grafted chitin and chitosan derivatives,

**Table 1. Potential Uses for Various Physical Forms of Chitin and Chitosan[28]**

| | |
|---|---|
| Beads | Coatings |
| metal chelation | surface modifications |
| wastewater treatment | textile finishes |
| drug delivery | seed coatings |
| enzyme immobilization | paper sizing |
| Fibers | Shaped Objects |
| medical textiles | orthopedics |
| sutures | contact lenses |
| Absorbent Powders | Films |
| wastewater treatment | membranes |
| animal feed additive | wound care |
| microcrystalline form | packaging |
| pharmaceutical/medical | |
| Solutions /Gels | |
| cosmetic | |
| wastewater treatment (cationic flocculent) | |

accompanied by product yields of both graft and homopolymer.

## *IV. Grafting of Chitin and Chitosan*

The chemistry discussed below will be divided into subsections based on the different types of initiators used in synthesizing the grafted derivatives. Graft yields (%G) will be reported based on the weight of chitin and chitosan trunk polymer charged as shown in eq 10.

$$\%G = \frac{(\text{weight of graft copolymer}) - (\text{weight of trunk polymer})}{(\text{weight of trunk polymer})} \times 100 \quad (10)$$

Depending on how the yields were reported in the literature, homopolymer (%H) will either be quantified based on the weight of total polymer formed (eq 11) or on the weight of monomer charged (eq 12).

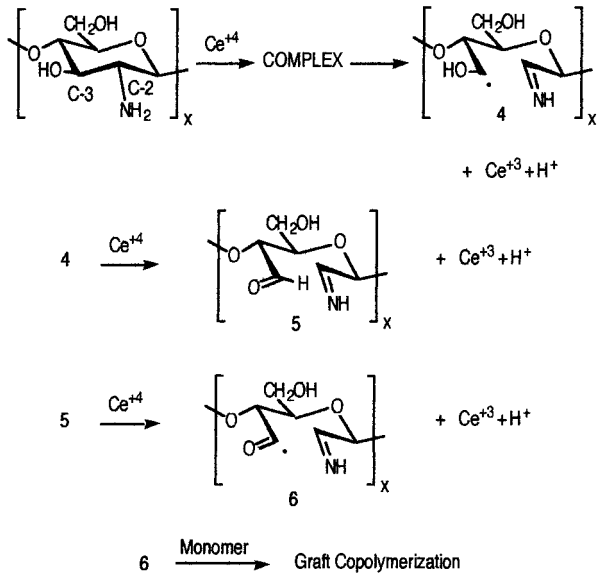
$$\%H = \frac{(\text{weight of homopolymer})}{(\text{weight of polymer grafted}) + (\text{weight of homopolymer})} \times 100 \quad (11)$$

$$\%H = \frac{(\text{weight of homopolymer})}{(\text{weight of monomer charged})} \times 100 \quad (12)$$

### A. Ceric Ion Initiation

Cerium in its tetravalent state is a versatile oxidizing agent that through various redox reactions with many different organic substrates can create free radicals capable of initiating vinyl polymerizations.[35] One of the more classic applications of ceric ion initiation is in the graft copolymerization of cellulose with vinyl monomers.[36,37] Typically ceric ion initiation is performed under acidic aqueous conditions. Acid concentration is believed to affect the rate of polymerization initiated by the ceric ion, but the relationship depends on the type of acid used.[36] For instance, the following equilibrium, shown in eq 13, is observed in aqueous perchloric acid solutions

**Scheme 3. Proposed Reaction Mechanism for Macroradical Production on the Chitosan Backbone Using Ceric Ion Initiation[38]**




where the ceric ion concentration is dependent upon the acid concentration.

$$Ce^{4+} + H_2O \rightleftharpoons CeOH^{3+} + H^+ \quad (13)$$

Generally aqueous ceric ion initiations are performed under acidic conditions to promote higher concentrations of $Ce^{4+}$.

The similarities in the chemical structures of chitin and chitosan with cellulose led to the use of ceric ion initiation for the synthesis of grafted chitin and chitosan derivatives. The mechanism of initiation for chitosan at 40 °C (the mechanism for chitin was not proposed) is believed to begin with a complex formation of the $Ce^{4+}$ ion with the primary amine at the C-2 position and the hydroxyl group at the C-3 position, based on work conducted with model compounds.[38,39] The radicals responsible for the initiation of grafted polymer chains using vinyl monomer are produced from the complex by the series of reactions shown in Scheme 3. At higher temperatures (i.e., 90 °C), it is proposed that the imine moiety in structure **4** is further hydrolyzed in the aqueous acidic condi-

**Table 2. Optimal Grafting and Homopolymer Yields Using Ceric Ion Initiation with Chitin and Chitosan[a]**

| monomer | trunk polymer | % grafting[b] | % homopolymer[c] |
|---|---|---|---|
| 4-VP[e] | chitosan | ~300 | d |
| AAM[f] | chitosan | 30−40 | d |
| AA[g] | chitosan | 50−60 | 10 |
| MAA[g] | chitosan | 50−60 | 10 |
| MA[h] | chitin | 500−600 | 20 |
| MMA[i,j] | chitin | 300−500 | d |
| AAM[k] | chitin | 200−250 | d |
| AA[l] | chitin | ~45 | d |

[a] 4-VP = 4-vinylpyridine, AAM = acrylamide, AA = acrylic acid, MAA = methacrylic acid, MA = methyl acrylate, MMA = methyl methacrylate. [b] Percent yield based on weight of trunk polymer. [c] Percent yield based on weight of total polymer formed. [d] Homopolymer was produced but not quantified. [e] Caner, H.; Hasipoglu, H.; Yilmaz, O.; Yilmaz, E. *Eur. Polym. J.* **1998**, *34* (3/4), 493. [f] Kim, K. H.; Kim, K. S.; Shin J. *Polymer (Korea)* **1987**, *11* (2), 133. [g] Shantha, K. L.; Bala, U.; Rao, K. P. *Eur. Polym. J.* **1995**, *31* (4), 377. [h] Lagos, A.; Yazdani-Pedram, M.; Reyes, J.; Campos, N. *J. Macromol. Sci., Pure Appl. Chem.* **1992**, *A29* (11), 1007. [i] Ren, L.; Miura, Y.; Nishi, N.; Tokura S. *Carbohydr. Polym.* **1993**, *21*, 23. [j] Ren, L.; Goto, Y.; Kaneko, H.; Shirai, A.; Nishi, N.; Nishimura, S.; Yamagishi, A.; Tokura, S. *Polym. Int.* **1994**, *35*, 303. [k] Kurita, K.; Kawata, M.; Koyama, Y.; Nishimura, S. *J. Appl. Polym. Sci.* **1991**, *42*, 2885. [l] Furlan, L.; de Favere, V. T.; Laranjeira, M. C. M. *Polymer* **1996**, *37* (5), 843.

tions to the corresponding aldehyde, whereby oxidation to an acyl radical, similar to the oxidation of **5** to **6**, gives another site capable of initiating a grafted polymer chain.

As with cellulose, the ceric ion has been a useful initiation method for synthesizing grafted chitin and chitosan derivatives with typical vinyl monomers. Moderate to excellent yields accompanied with various amounts of homopolymer are encountered. Table 2 provides some optimal yields of both grafted product and homopolymer as reported for various monomer and trunk polymer systems.

An interesting technique used for cellulose grafting, which has not been exploited on chitin and chitosan trunk polymers, is that of ceric ion pretreatment. Pretreatment has been performed by placing cellulosic substrates in aqueous ceric solutions at room temperature for given periods of time, removing the cellulose, and washing it with water to remove excess ceric ions. By subsequently placing the treated substrates in solutions where monomer is dissolved in benzene,[40] toluene,[41] or water,[42] efficient graft copolymerizations, with regard to obtaining low quantities of homopolymer, have been conducted. Pretreatment allows absorption of the ceric solution into the cellulose to promote a more uniform grafting. Removing extraneous ceric ions from the surface is believed to decrease the amount of side reactions with organic substrates in the medium, other than cellulose, which could lead to homopolymerization.

## B. Fenton's Reagent

Chitosan has been graft copolymerized with vinyl monomers using Fenton's reagent as the means of initiation.[43,44] Fenton's reagent involves a redox reaction between the ferrous ion and hydrogen peroxide, producing hydroxyl radicals. These radicals are believed to be responsible for creating the macroradicals

**Scheme 4. Radical Formation by Means of Fenton's Reagent in an Aqueous Environment[43]**

$$H_2O_2 + Fe^{+2} \longrightarrow \cdot OH + OH^- + Fe^{+3}$$

$$\cdot OH + Fe^{+2} \longrightarrow OH^- + Fe^{+3}$$

$$\cdot OH + H_2O_2 \longrightarrow H_2O + \cdot OOH$$

$$\cdot OOH + H_2O_2 \longrightarrow \cdot OH + O_2 + H_2O$$

on the chitosan backbone, by means of hydrogen abstraction, that initiate the growth of grafted chains with various monomers. Scheme 4 provides the proposed mechanism for hydroxyl radical formation using Fenton's reagent in an aqueous medium.

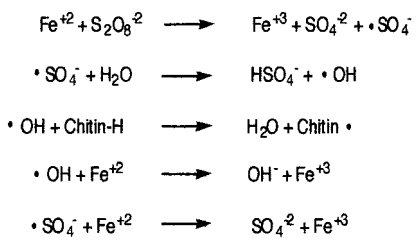
Methyl methacrylate was grafted with yields of 400−500% based on weight of chitosan with homopolymer yields of approximately 20−30% based on weight of total polymer formed.[43] Methyl acrylate has been successfully grafted with yields of 250−300% based on weight of chitosan, while homopolymer was produced in the range of 15−20% based on weight of monomer charged.[44]

Although hydrogen peroxide alone could be an adequate initiator for graft copolymerization, there are reasons why reducing agents such as $Fe^{2+}$ are used for grafting onto chitosan. In addition to the higher yield of radical production at much lower temperatures via the redox reaction, the chelating properties of chitosan with metal ions tend to promote hydroxyl radical formation in the vicinity of the chitosan in order to increase macroradical yields rather than homopolymer initiation.

Having $Fe^{2+}$ complexed with the trunk polymer was performed on chitin where the chelating properties were enhanced through the addition of thiocarbonate sites along the chitin backbone via the xanthate process (aqueous NaOH and $CS_2$).[45] After treating the chitin thiocarbonate derivative with $Fe^{2+}$, the complex (Chitin-O$-CS_2^-)_2Fe^{2+}$ was formed. The decomposition of the complex leads to free $Fe^{2+}$, which is believed to react with hydrogen peroxide as shown in Scheme 4 to produce hydroxyl radicals in solution that subsequently create chitin macroradicals upon hydrogen abstraction. Grafting yields on the order of 80% and 40% based on weight of chitin were obtained with this process using acrylonitrile and acrylic acid, respectively. In both cases, homopolymer was obtained but not quantified.

A variation of Fenton's reagent has been investigated as an alternative method for graft copolymerization of chitin and chitosan with various vinyl monomers. In this method, potassium persulfate (KPS) and ferrous ammonium sulfate (FAS)[46] are combined in a redox reaction that produces radicals in solution that are capable of initiating graft copolymerization. The proposed mechanism is shown in Scheme 5, where it is the hydroxyl radicals ultimately formed that are believed to be responsible for creating macroradicals. Methyl methacrylate was grafted onto chitin with this system at approximately 300−350% based on the weight of original chitin charged, where 40−50% of the monomer was homopolymerized. This work also used potassium persulfate alone for the graft copolymerization of chitin. The persulfate anion

**Scheme 5. Mechanism for Macroradical Production on the Chitin Backbone Using the $Fe^{2+}$/Persulfate Redox System[46]**




can undergo homolytic cleavage by heating to form sulfate anion radicals. The sulfate anion radicals react as shown in Scheme 5 such that some chitin macroradicals are subsequently created. In comparison to the FAS−KPS system, persulfate alone was only able to achieve approximately 80−90% graft yield on weight of chitin while producing the same yields of homopolymer.

Potassium persulfate was used to graft chitosan with vinyl pyrrolidone monomer.[47] Graft yields of 250−300% based on weight of chitosan were obtained accompanied by 10−20% homopolymer yield based on weight of monomer charged. An interesting reaction mechanism with the chitosan/persulfate system has been proposed by Wang et al.,[48] where the chitosan's free amine reacts directly with the persulfate anion to yield R−NH, $OSO_3H$, and $SO_4^{2-}$.

Work outlined in Table 3, where chitosan was grafted with methyl methacrylate and methyl acrylate, compares KPS initiation to that of initiation by KPS coupled with various other reducing agents.[49] No reference was made to a mechanism where the persulfate reacts specifically with the chitosan as proposed by Wang et al.,[48] so it is assumed that the general mechanism proceeds as in Scheme 5, where the other reducing agents ($CuCl_2$, $MnCl_2$, etc.) could be substituted for $Fe^{2+}$.

## C. $\gamma$-Radiation

Free radicals can be generated by complicated mechanisms when organic substrates are subjected to high-energy radiation, such as $\gamma$-radiation.[50] The mechanism of radical production has the following characteristics: radicals are produced by means of electron abstraction to form radical cations, typically radical formation is concentrated along the path of the incident radiation beam, and radical generation is fairly unselective. Although it appears to have a number of disadvantages in terms of its lack of specificity, it is a convenient method because there are no "synthetic" steps to be performed. Thus, it is often used for the initiation of vinyl polymerizations by both radical (predominantly) and ionic mechanisms.[51]

Chitin and chitosan have been graft copolymerized with various monomers by means of $\gamma$-radiation. Typically chitin and chitosan substrates are exposed to $\gamma$-radiation, creating macroradicals that when in the presence of vinyl monomers lead to graft copolymerizations. Shigeno et al. graft copolymerized styrene onto chitin and chitosan by means of $\gamma$-radiolysis,[52] where yields of 100% graft on weight of trunk polymer could be achieved with 25% of the total polymer formed being polystyrene homopolymer. Singh and Ray graft copolymerized 2-hydroxyethyl methacrylate[53] and *N,N*-dimethylaminoethyl methacrylate[54] onto chitosan using $\gamma$-radiolysis where the yields of graft were approximately 100% and 40−60%, respectively, based on weight of chitosan. In this work, homopolymer was produced but not quantified.

## D. Various Radical and Photoinduced Methods

Work by Kojima et al., being one of the earliest publications addressing the graft copolymerization of chitin, utilized tributyl borane (TBB) as the means of initiation.[55] According to Kojima et al., the alkylborane-initiated polymerizations of various vinyl monomers in the presence of oxygen occur by means of a free radical mechanism, prompting the investigation of this initiator for the grafting of chitin with methyl methacrylate. The details provided in regard to the grafting mechanism were the following: "(1) solvation of water to chitin, (2) formation of the complex from solvated chitin and TBB, and (3) graft initiation by free radicals from the complex".[55] Water was necessary to obtain a grafted derivative. Methyl methacrylate was grafted onto chitin at 40% based on weight of monomer charged with this method. Homopolymer yields were on the order of 50% based on total weight of polymer formed.

As shown by several examples in Table 4, chitin and chitosan have been graft copolymerized using initiators such as azobisisobutyronitrile (AIBN), ammonium persulfate (APS), and hydrogen peroxide ($H_2O_2$). These initiators are commonly used to polymerize vinyl monomers with the addition of heat or light. The first radicals produced by these systems occur from homolytic bond scissions of the initiator,

**Table 3. Graft and Homopolymer Yields on Chitosan as a Function of Initiator System and Monomer[49,a]**

| monomer | initiator system | % graft product[b] | % homopolymer[c] |
|---|---|---|---|
| MMA | KPS | 268 | 37 |
| MMA | KPS/$CuCl_2$ | 197 | 29 |
| MMA | KPS/$MnCl_2$ | 489 | 16 |
| MMA | KPS/ammonium oxalate | 397 | 29 |
| MMA | KPS/ammonium tartrate | 388 | 31 |
| MA | KPS | 281 | 63 |
| MA | KPS/$CuCl_2$ | 48 | 87 |
| MA | KPS/$MnCl_2$ | 335 | 22 |
| MA | KPS/ammonium oxalate | 511 | 4 |
| MA | KPS/ammonium tartrate | 339 | 40 |

[a] MMA = methyl methacrylate, MA = methyl acrylate. [b] Based on weight of chitosan. [c] Based on weight of total polymer formed.

**Table 4. Product Yields of Grafted Chitin/Chitosan and Homopolymer for Various Initiator Systems[a]**

| trunk polymer | monomer | initiator | %G[b] | %H[c] |
|---|---|---|---|---|
| chitosan | VA[f] | thermal w/AIBN | 10 | d |
| chitosan | MA[f] | thermal w/AIBN | 20 | d |
| chitosan | MMA[f] | thermal w/AIBN | 65 | d |
| chitosan | AN[f] | thermal w/AIBN | 10 | d |
| chitosan | MMA[g] | noncatalytic photoinduced[e] | 300 | 30−40 |
| chitosan | MMA[g] | photolysis w/AIBN | 150 | 60 |
| chitosan | MMA[g] | photolysis w/$Ph_2CO$ | 140 | 40 |
| chitosan | MMA[g] | thermal w/APS | 300 | 50 |
| chitosan | MMA[g] | thermal w/$H_2O_2$ | 300 | 50 |
| chitin | MMA[h] | noncatalytic photoinduced[e] | 150 | 50 |
| chitin | MMA[h] | photolysis w/AIBN | 60 | 90 |
| chitin | MMA[h] | photolysis w/$H_2O_2$ | 70 | 50 |
| *O*-acetyl chitin | MMA[i] | photolysis of *O*-acetyl | 500 | 20−30 |

[a] VA = vinyl acetate, MA = methyl acrylate, MMA = methyl methacrylate, AN = acrylonitrile. [b] Percent grafted product based on weight of trunk polymer. [c] Percent yield of homopolymer based on weight of total polymer formed. [d] Homopolymer was obtained but not quantified. [e] This method of initiation involved the irradiation of only chitosan, solvent, and monomer with light of 253 nm where the proposed method of initiation was the removal of the amine group of chitosan by photolysis. [f] Blair, H. S.; Guthrie, J.; Law, T.; Turkington, P. *J. Appl. Polym. Sci.* **1987**, *33*, 641. [g] Takahashi, A.; Sugahara, Y.; Horikawa, Y. *Sen-I Gakkaishi* **1987**, *43* (7), 362. [h] Takahashi, A.; Sugahara, Y.; Hirano, Y. *J. Polym. Sci., Polym. Chem. Ed.* **1989**, *27*, 3817. [i] Morita, Y.; Sugahara, Y.; Takahashi, A.; Ibonai, M. *Eur. Polym. J.* **1997**, *33* (9), 1505.

whereby these radicals subsequently react with the monomer to initiate the polymerization. For typical graft copolymerization, these radicals provided by the initiator, in addition to reacting directly with vinyl monomer, abstract hydrogens from chitin or chitosan creating macroradicals that are capable of initiating a grafted chain with vinyl monomers.

In attempts to produce conductive chitosan derivatives, chitosan was grafted with aniline by means of an initiating system comprised of $(NH_4)_2S_2O_8$ and aqueous HCl;[56] however, little detail was given in regard to the grafting mechanism. Neither grafted product nor homopolymer were quantified, but some homopolymer was removed.

Chitosan, acylated with maleic anhydride, was grafted and ultimately cross-linked with acrylamide by means of $(NH_4)_2S_2O_8$ initiation.[57] The reaction proceeded by means of a free radical mechanism where the maleic vinyl group provided the site for radical formation on the chitosan. This work mainly described the properties of the grafted products.

Iodochitin (chitin where the C-6 position is substituted with an iodo group) was graft copolymerized with styrene using a cationic mechanism induced in the presence of a Lewis acid and a free radical mechanism induced by UV radiation.[58] The Lewis acid is believed to remove $I^-$ by the cationic mechanism, leaving a positive charge on the C-6 carbon that is then capable of initiating cationic polymerization. The UV light gives rise to a homolytic cleavage of the (C-6)−I bond so that a macroradical is produced on chitin capable of initiating graft copolymerization. Grafting yields from the cationic mechanism were reported to be in the range of 800% based on weight of chitin. Substantial homopolymer was formed but was not reported quantitatively. The radical mechanism provided much lower yields of grafting as compared to the cationic mechanism (50−60% based on weight of chitin), but it was claimed that almost no homopolymer was formed.

Mercaptochitin (C-6 position) was grafted with methyl methacrylate[59,60] to give extremely high yields of graft copolymer, sometimes as high as 900−1000% graft based on weight of chitin. The premise behind this mechanism is that the thiol group, typically used as a chain transfer agent in vinyl polymerizations, has the ability to easily dissociate into free radicals. The mercapto group, in the presence of heat and vinyl monomer, undergoes homolytic scission of the S−H bond, providing the site for free radical graft copolymerization without the need of a co-initiator. Although the extent of homopolymerization was not mentioned, it was stated that homopolymer had to be extracted from the product after the reaction was completed.

## E. Nonradical-Based Mechanisms

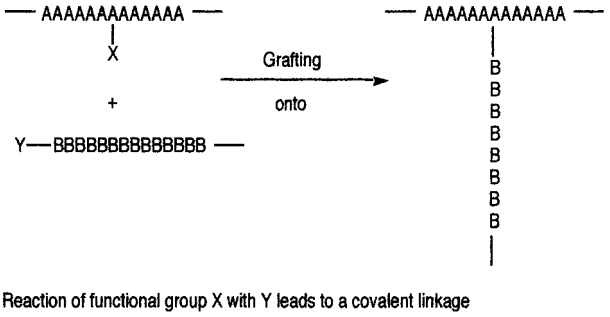
The majority of the grafting methods discussed thus far have involved free radical-based systems. Radical grafting is a more versatile technique in the sense of utilizing one basic mechanism with many different vinyl monomers for obtaining a wide range of hybrid polymer properties. However, alternative methods have been developed for chitin and chitosan grafting that involve ring-opening and "grafting onto" mechanisms, which will be presented in the following sections in order to complete the review of chitin/chitosan grafting.

### *1. Ring-Opening Methods*

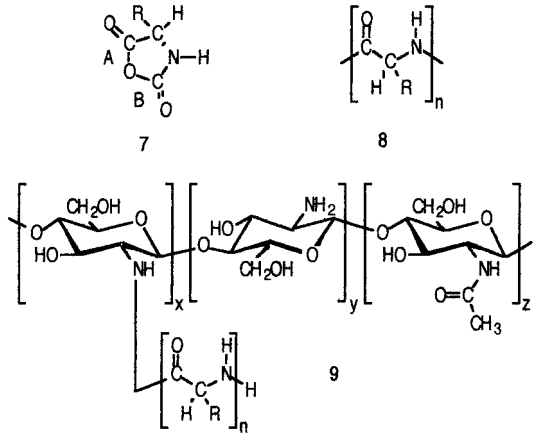
The main type of monomers used to synthesize the grafted derivatives of chitin and chitosan by ring-opening methods is that of various *N*-carboxyanhydrides (NCA). NCA was developed by Leuchs and Geiger[61] and improved upon by Woodward and Schramm[62] for the synthesis of poly-α-amino acids. Partially deacetylated chitins have been grafted with D,L-alanine NCA,[63] γ-methyl L-glutamate NCA,[64,65] and L-alanine.[66] Daly and Lee[67] discuss the grafting of various amino acids onto natural and synthetic polymers using NCAs.

NCAs have the general structure **7** and can undergo ring-opening polymerizations with the evolution of carbon dioxide to yield a polymer having repeat structure **8**.[68] The free amine of partially

**Scheme 6. Representation of Telechelic Grafting where Polymer B's Chain End Is Bonded to the Polymer A Backbone to Yield an A-*g*-B Derivative**




deacetylated chitin is believed to initiate the graft copolymerization by means of nucleophilic attack upon carbonyl A of **7**, ultimately creating the grafted chitin derivative **9**. Generally the grafting of partially deacetylated chitin with NCA proceeded with high efficiency in the sense that little homopolymer was observed. One of the advantages with this method is that side chain lengths can be regulated as a function of NCA concentration; however, DPs are usually lower than 20 units.

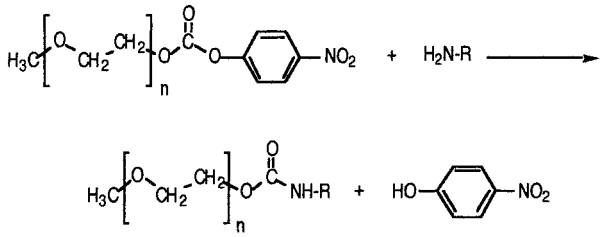



### *2. "Grafting Onto" Methods*

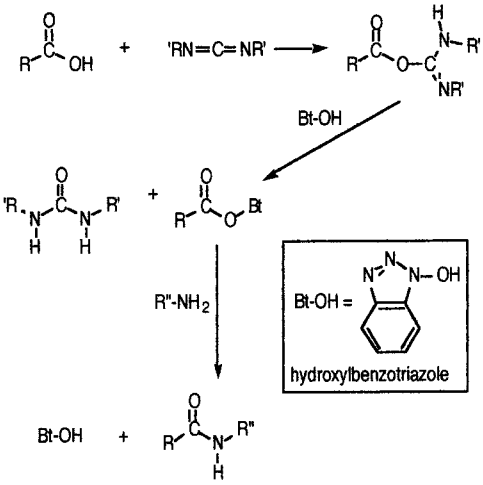
Grafting with telechelic polymers provides an alternative method, commonly referred to as "grafting onto", for synthesizing hybrid branched architectures.[1] Telechelic polymers have been defined as those "containing one or more functional end groups that have the capacity for selective reaction to form bonds with another molecule".[69] Unlike the classic grafting techniques where the grafted chain is grown from the trunk polymer by the continual addition of monomer to the growing chain end, "grafting onto" connects homopolymer chains A and B (Scheme 6) by covalently bonding the chain end of polymer B with a particular site on polymer A's backbone.

Methoxy-poly(ethylene glycol) (PEG)-*p*-nitrophenyl carbonate (MW = 5000) was used to acylate chitosan free amine groups through a urethane linkage.[70] Scheme 7 provides the reaction for urethane formation with primary amines and methoxy-(PEG)-*p*-nitrophenyl carbonate. Grafting yields were 80−90% based on weight of chitosan, where the grafted derivatives were soluble in aqueous solutions at pH 6.5, contrary to highly deacetylated chitosan. Methoxy-poly(ethylene glycol) acid ($M_n$ = 5000) was activated with a carbodiimide/hydroxylbenzotriazole technique, used in peptide synthesis,[72] to subsequently acylate chitosan free amine groups.[73] Scheme 8 provides the mechanism for activating carboxylic acid derivatives with the carbodiimide/hydroxylbenzotriazole technique in order to acylate primary amine groups. Chitosan grafted with PEG side chains were obtained with degrees of N-substitution ranging from 0.02 to 0.55, where degrees of N-substitution greater than 0.10 were observed to be water soluble after ultrasonication.

**Scheme 7. Urethane Bond Formation Using Methoxypolyethylene Glycol-*p*-nitrophenyl Carbonate to Acylate Primary Amines[71]**




**Scheme 8. Carboxylic Acid Activation Using a Carbodiimide/Hydroxylbenzotriazole System for Primary Amine Acylation[72]**

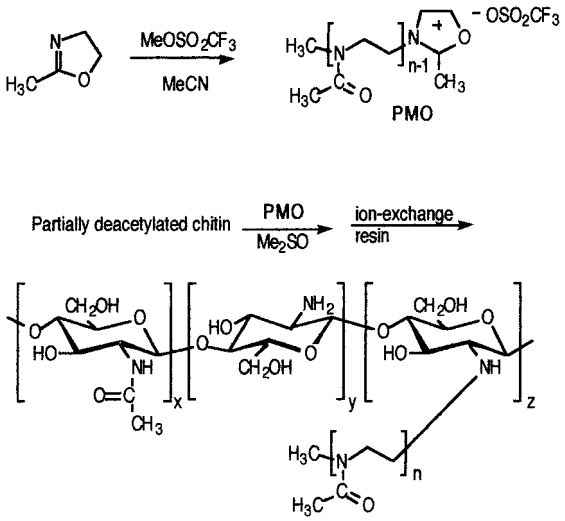



Living poly(2-methyl-2-oxazoline) telechelic polymers have been grafted onto partially deacetylated chitins[74−78] where full degrees of N-substitution of available amine groups have been obtained with grafted chain DPs ranging from 8 to 20 units.[77] The general reaction for grafting partially deacetylated chitin, including the synthesis of living poly(2-methyl-2-oxazoline), is provided in Scheme 9. These grafted derivatives are miscible with poly(vinyl chloride) to varying degrees[75−77] and soluble in water, dimethyl formamide, and dimethyl sulfoxide, with partial solubility in chloroform, acetonitrile, and methanol.[74]

## *V. Critique of Radical Grafting Methods*

The radical-based grafting chemistry outlined in sections IV.A−D illustrates the level of homopolymer that can be obtained when conducting vinyl graft copolymerizations with different techniques. In terms of chain growth polymerizations, free radical-based

**Scheme 9. Synthesis of Living Poly(2-methyl-2-oxazoline), PMO, Followed by Its Use To Graft Partially Deacetylated Chitin.[74] The Grafted Derivative Has Also Been Produced in Toluene where PMO Was Synthesized by Initiation with Methyl-*p*-toluene Sulfonate[78]**




mechanisms classically have been a more versatile means of synthesizing macromolecules with a variety of properties due to the wide range of vinyl monomers susceptible to radical polymerizations. Synthesizing a grafted derivative with free radical techniques can be an extremely complicated process. In polymer synthesis, the characterization of the final product (chemical structure, tacticity, molecular weight, molecular weight distribution, yield, etc.) is crucial in understanding not only the mechanistic details of the chemistry involved, but also the structure−property relationships exhibited by the polymer.

Homopolymer, typically produced during "grafting from" syntheses, signals monomer wastage and makes graft copolymer characterization an even more difficult task. In regard to grafting cellulose with vinyl monomers, Stannett discussed potential problems created by homopolymer such as its removal and disposal, important issues if considering large-scale production.[79] The common technique for evaluating graft and homopolymer yields involves extraction of the grafted sample to constant weight with a solvent for the homopolymer that is correspondingly a nonsolvent for the original trunk polymer. This procedure is fairly straightforward; however, yield characterization can be further complicated if trunk and grafted chains are solubilized in the reaction medium. For example, negative grafting yields were observed with poly(ether−urethanes) heterogeneously grafted with acrylic acid and methyl methacrylate.[80] There is an obvious motivation toward synthetic schemes that reduce or ideally eliminate homopolymer formation. This achievement would allow the production of grafted derivatives with potentially lower monomer concentrations and facilitate more efficient graft copolymer characterizations.

Regarding free radical grafting, an ideal mechanism (in terms of homopolymer elimination) could be envisioned as follows: (1) the only free radicals created for initiation are specifically produced on the trunk polymer backbone, (2) the macroradicals initiate a grafted polymer chain that propagates by continual monomer addition without the occurrence of chain transfer of the radical from the chain end to some species in the medium, and (3) termination occurs by combinations of coupling, disproportionation, and addition of inhibitors. These steps would require the radical to remain bonded to the graft copolymer throughout the entire reaction. Any reactive radicals that are not chemically attached to the grafted derivative have the potential of initiating homopolymerization. Homopolymer should thus be eliminated barring any thermal polymerizations in solution, for example, as a result of various peroxides formed from trace amounts of oxygen or self-initiated thermal polymerizations as in the case of styrene.[81]

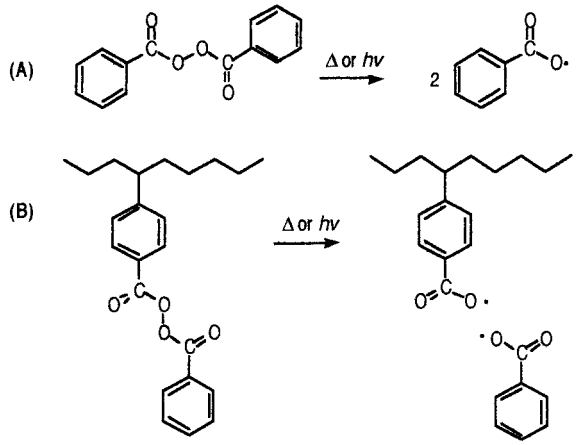
Although the above scenario is ideal, control over specific macroradical creation and chain transfer are nevertheless the keys toward synthesizing a grafted derivative of any trunk polymer with minimal homopolymerization. Considering the radical initiating techniques utilized for chitin and chitosan grafting, the ceric ion is the most widely used technique which offers the greatest degree of specificity in regard to macroradical formation. Most of the chemistry discussed in sections IV.B−D generates radicals first in solution that subsequently create macroradicals. It should be noted however that the ceric ion is capable of radical generation with a wide variety of compounds;[35] therefore, it is possible that various other side reactions could yield different radicals in the medium, encouraging homopolymerization. Moreover, none of the systems discussed are able to control the level of chain transfer of growing grafted chains to other species in the medium due to their conventional free radical character. Another consequence of their conventional nature is that true control over the grafted chain molecular weight and dispersity would be difficult. Thus, alternative methods which address all of these issues are necessary for grafting chitin/chitosan and other important trunk polymers. The remaining portion of this review will be devoted to alternative initiating chemistries which offer potential improvements in these areas.

## *VI. Redox Initiation Methods which Exhibit Conventional Free Radical Polymerization Character*

In conventional free radical polymerizations, the more common method of radical generation results from homolytic dissociation of compounds such as benzoyl peroxide with the application of heat or light giving two radicals per decomposition (see Scheme 10A).[82,83] Hypothetically if the peroxide moiety were bonded to a trunk polymer as shown in Scheme 10B, the homolytic cleavage of the peroxide would produce a macroradical but would also unfortunately yield a radical that is not bonded to the trunk polymer that is free to initiate homopolymerization.

The creation of macroradicals, and only macroradicals, requires initiating methods yielding one radical per reaction. A class of initiators with this feature are redox initiators. Redox initiators typically involve

**Scheme 10. (A) Homolytic Scission of Benzoyl Peroxide with the Application of Heat or Light. It Should Be Noted that the Radical Generated from Benzoyl Peroxide Is Believed To Undergo Further Decomposition To Yield $CO_2$ and a Phenyl Radical. (B) Radical Formation from Applying Heat or Light Using the Peroxide Group Attached to a Trunk Polymer**




two substrates or co-initiators reacting in such a way that one component is reduced while the other is oxidized, usually by a type of electron transfer, resulting in the generation of one radical bonded to one of the components.[83] The co-initiator concept can be applied to grafting by the incorporation of a specific site (co-initiator 1) on the trunk polymer backbone, whereby the addition of co-initiator 2 a radical is created on the trunk polymer backbone and nowhere else in the medium.

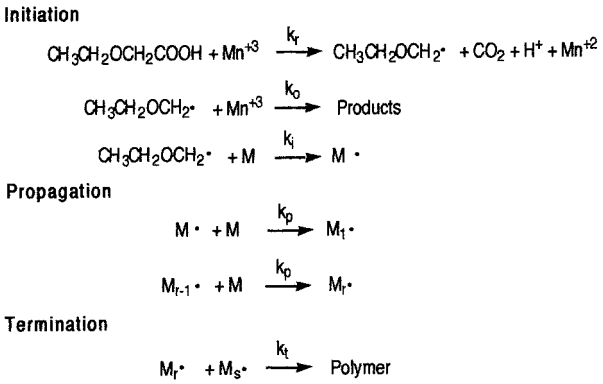
In the organic synthesis of lower molecular weight compounds, transition metals such as titanium, vanadium, iron, manganese, copper, and cobalt can be used as both oxidants and reductants (depending on the metal's valence) for the generation of carbon−carbon bonds via radical-based mechanisms.[84] Likewise, a large number of examples can be found in the literature where redox reactions involving transition metals as one of the co-initiators in bicomponent systems, in a variety of valence states, are used to generate radicals for the purpose of vinyl polymerizations.

Several reviews have addressed different types of radical-generating systems involving, for example, vanadium(V), manganese(III), and iron(III) transition metals including cerium(IV) from the lanthanide series (having been discussed earlier for chitin and chitosan grafting), that react with a variety of organic substrates through redox-based mechanisms which have been used for vinyl polymerizations (specifically toward grafting of silk and cellulose derivatives).[85−89] Adding to the information provided in these reviews, several examples from the more recent literature utilizing co-initiator redox-based systems will be discussed which could be used for specific macroradical formation while focusing on the mechanisms of radical formation.

## A. Manganese(III)

Manganese in its trivalent state is a powerful oxidizing agent capable of generating free radicals

**Scheme 11. Proposed Reaction Sequence for Radical Generation and Subsequent Vinyl Polymerization with Acrylamide (M) Using the Ethoxyacetic Acid/$Mn^{3+}$ Redox System[90]**




on a variety of organic substrates through redox mechanisms. Nayak and Lenka reviewed radical generation using Mn(III) to oxidize compounds such as malonic acid, cyclohexanone, and dimethyl sulfoxide,[85] while Samal et al. reviewed the mechanism of macroradical formation on cellulose with Mn(III).[89]

Studies have been conducted on other Mn(III) redox systems to elucidate some of the mechanistic features of radical formation for initiating vinyl polymerizations. For example, experiments have been conducted by Balakrishnan and Subbu[90] on a Mn(III)/ethoxyacetic acid redox-initiating system for the polymerization of acrylamide in an aqueous medium in the presence of $H_2SO_4$ and $NaHSO_4$. Scheme 11 provides the proposed reactions of radical generation for these polymerizations. Rate laws shown below for both the rate of polymerization ($R_p$), eq 14, and the rate of Mn(III) disappearance ($-R_m$), eq 15, were developed from the reactions in Scheme 11 and supported by the kinetic data (M = acrylamide and EAA = ethoxyacetic acid).

$$R_p = k_p[M]\left(\frac{k_r[EAA][Mn^{3+}]}{k_t}\right)^{1/2} \quad (14)$$

$$-R_m = k_r[Mn^{3+}][EAA] \quad (15)$$

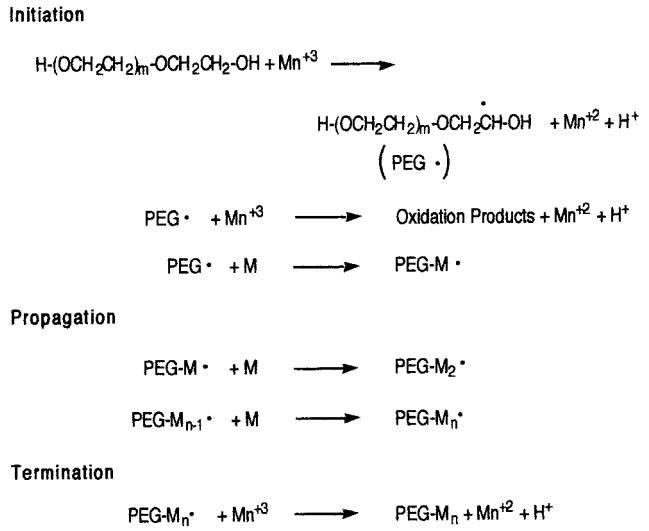
Equation 16 was developed for $\bar{X}_n$ in conjunction with the previous rate laws.

$$\bar{X}_n = \frac{k_p[M]^{1/2}(k_i[M] + k_o[Mn^{3+}])^{1/2}}{(k_r k_i k_t[EAA][Mn^{3+}])^{1/2}} \quad (16)$$

The mode of termination was believed to occur from only combination of the growing chains and not from further oxidation of the radical by Mn(III), as suggested and discussed elsewhere in other Mn(III) redox systems.[85] It was stated that obtaining linear plots of degrees of polymerization versus both $1/[EAA]^{1/2}$ (passing through the origin) and $1/[Mn^{3+}]^{1/2}$ (having a positive *y*-intercept) were key observations that helped to develop the proposed mechanism which included termination solely by coupling.

Balakrishnan et al.[91] conducted further polymerizations on acrylic acid (AA) and methacrylamide

**Scheme 12. Reaction Mechanism for the Block Copolymerization of Poly(ethylene glycol) with Acrylonitrile (M) Using Mn(III) as a Redox Initiator[92]**




(MAM) using the same initiating system. No differences were observed in the kinetics for either of the monomers. The same general mechanism was proposed as shown in Scheme 11 except the only suggested mode of termination was further oxidation of radical chain ends as shown in eq 17.

$$M_r^{\bullet} + Mn^{3+} \xrightarrow{k_t} \text{Polymer} + Mn^{2+} + H^+ \quad (17)$$

As a result, different rate laws for $R_p$ and $-R_m$ were obtained and are provided in eqs 18 and 19, respectively ([M] stands for either acrylic acid or methacrylamide concentrations).

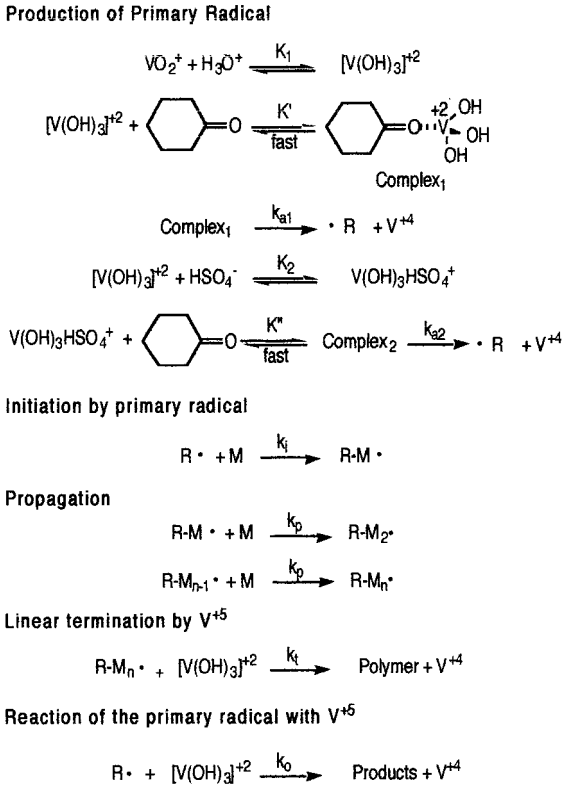
$$R_p = \frac{k_p k_r [EAA][M]}{k_t} \quad (18)$$

$$-R_m = 2k_r[Mn^{3+}][EAA] \quad (19)$$

The fact that the rate of polymerization was not affected by $[Mn^{3+}]$ was given as the justification for proposing termination solely by the $Mn^{3+}$ oxidation of radical chain ends, since the steady-state assumption of constant radical concentration was applied in the study. This is indicated by the factor of 2 introduced in the above expression for $-R_m$, eq 19, because the metal is consumed (according to the mechanism) in both the creation and removal of radicals. With the rates of radical creation and removal being equated under the steady-state assumption, the total rate of $Mn^{3+}$ disappearance can be described as twice the rate of radical generation. No explanation was given as to why $Mn^{3+}$ participated in the termination of acrylic acid and methacrylamide polymerizations by radical oxidations and not in those of acrylamide.

Poly(ethylene glycol) has been block copolymerized with acrylonitrile using Mn(III) as a redox initiator to create radicals on the PEG chain end by oxidation of the primary alcohol end group as shown in Scheme 12.[92] Cakmak continued work with this redox system by synthesizing PEG block copolymers with both methyl methacrylate and acrylamide monomers[93,94] and has reviewed the general synthesis of PEG block copolymers using a variety of techniques, including Mn(III) redox initiation.[95]

**Scheme 13. Reaction Sequence of Vinyl Polymerization (M = vinyl monomer, acrylonitrile) Using Redox Radical Generation with $V^{5+}$/Cyclohexanone Initiating System[96]**




## B. Vanadium(V)

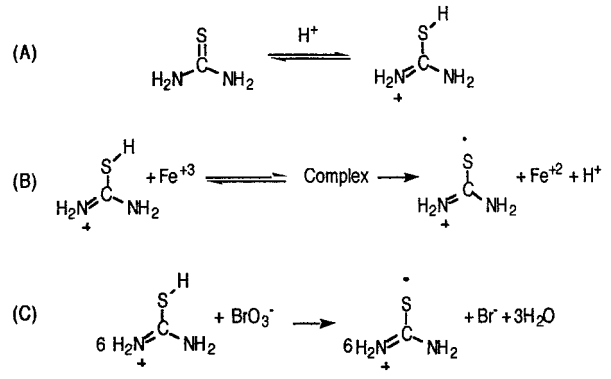
The redox mechanisms and kinetics of radical generation using $V^{5+}$ with reducing agents such as thiourea, ethylene glycol, silk fibers, and cellulosic materials have been reviewed.[85−89] Earlier work by Mohanty et al.[96] investigated the mechanism and kinetics of the vanadium(V)/cyclohexanone redox system capable of initiating vinyl polymerization (acrylonitrile) in an aqueous sulfuric acid medium. In conjunction with the mechanism provided in Scheme 13, the rate of polymerization ($R_p$) and rate of $V^{5+}$ disappearance ($-R_V$) shown in eqs 20 and 21, respectively, were derived in support of the kinetic data

$$R_p = \frac{k_p k'[CH][M]^2}{k_t\left\{[M] + \left(\frac{k_o}{k_i}[V^{5+}]\right)\right\}} \quad (20)$$

$$-R_V = 2k'[CH][V(OH)_3{}^{2+}] \quad (21)$$

where $k' = K_1K'k_{a1} + K_1K_2K''k_{a2}[HSO_4^-]$, CH = cyclohexanone, and M = monomer (acrylonitrile). Skaria et al.[97] applied this system with the intention of synthesizing a macroporous polymeric redox initia-

**Scheme 14. (A) Equilibrium Reaction between Thiourea and Isothiourea under Aqueous Acidic Conditions. Production of Sulfur-Based Radicals Capable of Initiating Vinyl Polymerization via a Redox Reaction between Isothiourea and Either $Fe^{3+}$ (B) or $BrO_3^-$ (C)[88]**




tor for the free radical polymerization of acrylamide in an aqueous sulfuric acid medium. Beads comprised of a glycidyl methacrylate−ethylene glycol dimethacrylate copolymer were modified with the addition of carboxylic acid moieties. With the carboxylic acid groups present, $V^{5+}$ was complexed with the copolymer whereby the addition of cyclohexanone promoted the creation of free radicals in the presence of acrylamide, yielding polyacrylamide chains with viscosity average molecular weights in the range of $3.5-13.3 \times 10^5$ g/mol.

## C. Thiol and Thiourea with Iron(III) and $KBrO_3$

The use of $Fe^{3+}$ and $KBrO_3$ to generate free radicals by the oxidization of thiol groups via redox-based mechanisms has been discussed in terms of their abilities to initiate vinyl polymerizations in an aqueous environment.[85,87,88,98] Under aqueous acidic conditions (typically $HClO_4$ or HCl), thiourea is protonated to the corresponding isothiourea (Scheme 14A), and it is this latter thiol species which is involved in the redox reactions with either $Fe^{3+}$ (Scheme 14B) or $KBrO_3$ (Scheme 14C) to produce sulfur-based radicals.[88]

The free radical nature of this system is supported by ESR spectroscopy spin trapping experiments conducted by Saha and Greenslade.[99] Methyl acrylate and methyl methacrylate were polymerized with $Fe^{3+}$/thiourea and $KBrO_3$/thiourea redox initiators in aqueous HCl, and the propagating chain radicals were trapped with the addition of 2-methyl-2-nitroso propane (MNP). Spin-trapped ESR spectra using both types of initiators were claimed to be comparable with those initiated by AIBN.[100]

Cysteine, an amino acid exhibiting a primary thiol group, has been used in conjunction with $KBrO_3$ to initiate the polymerization of acrylamide under aqueous acidic conditions.[101] An interesting aspect of this system that requires careful consideration when conducting radical polymerizations was realized by monitoring the kinetics of this system. Generally thiol groups are excellent chain transfer agents and are commonly used to reduce molecular weights in vinyl polymerizations to yield lower viscosities for easier bulk processing. In calculating the chain transfer constant of cysteine to be on the order of 0.4, it was suggested that cysteine is involved not only in radical generation, but also in promoting chain transfer of propagating radicals resulting in lower molecular weights of polyacrylamide.

One of the key steps in minimizing homopolymerization is the reduction of chain transfer. At first, this system might appear to be disadvantageous because one of the co-initiators also operates as a chain transfer agent. However, having mercapto moieties bonded to the trunk polymer, the addition of Fe(III) or $KBrO_3$ should yield specific macroradical formation, resulting in grafted polymer. Subsequent chain transfer from these growing grafted chains to attached mercapto groups would yield additional macroradical formation, not encouraging homopolymerization from *this* particular occurrence of chain transfer. It should be noted however that chain transfer to other substrates (those not bonded to trunk polymer) will still encourage homopolymer formation. Overall, the key to the successful utilization of this system for vinyl grafting is that the *only* mercapto groups in the system should be those bonded to the trunk polymer.

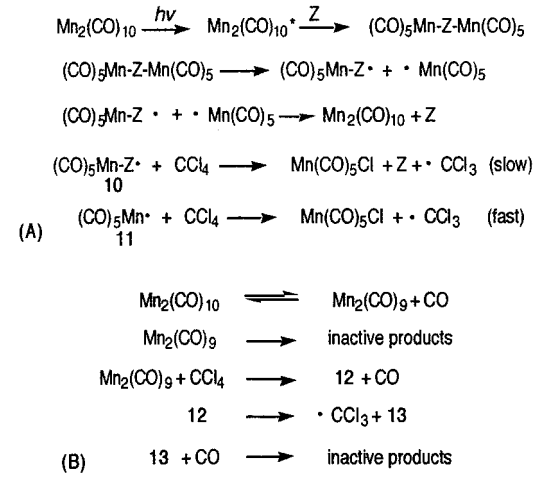
## D. Organohalide/Organometallic Co-initiation

Literature reviews by Bamford discuss initiator systems based on transition-metal complexes with ligands such as carbonyls, hexa-aryl isocyanides, triphenylphosphine, and triphenyl phosphite.[102,103] These types of initiators, whether activated thermally or by photosensitization, interact with a co-initiator, most commonly an organohalide (Cl or Br), whereby the metal complex transfers an electron to the carbon−halogen bond. Typically the electron transfer causes the carbon−halogen bond to cleave to a carbon-based radical (capable of initiating vinyl polymerization) and a halide anion (which is subsequently complexed with the metal). Of the many different types of metal complexes discussed by Bamford, some of the features and mechanisms of $Mn_2(CO)_{10}$ and $Mo(CO)_6$ co-initiators will be presented below.

$Mn_2(CO)_{10}$ can react photochemically or thermally with various organohalides to yield carbon-based radicals upon removal of a halide substituent.[102,103] The irradiation of $Mn_2(CO)_{10}$ with near-UV and visible light in the presence of $CCl_4$ produces $Mn(CO)_5Cl$ in nearly quantitative yields (two molecules of $Mn(CO)_5Cl$ per $Mn_2(CO)_{10}$ reacted).[104] It is proposed that the Mn−Mn bond upon excitation undergoes a homolytic cleavage to yield two equivalents of $Mn(CO)_5$ metal radicals that are capable of abstracting the chlorine substituent to produce a carbon radical, at least in the case of organohalides such as $ClCH_2Ph$ and $Ph_3CCl$.

According to Bamford,[103] the photoinitiated mechanism (using 436 nm light) of the $Mn_2(CO)_{10}/CCl_4$ system for polymerizations is one where the metal carbonyl is divided into two fragments (Scheme 15A). The fragments can interact with the halogen or eventually regenerate the original metal complex. An after-effect can also be observed in that $Mn_2(CO)_{10}$

**Scheme 15. (A) Proposed Reaction Scheme of Radical Generation with the $Mn_2(CO)_{10}/CCl_4$ System under Photoinitiating Conditions in the Presence of Acetylacetone (Z).[103] (B) Thermal (80 °C) Radical Generation Proposed for the $Mn_2(CO)_{10}/CCl_4$ System[106]**

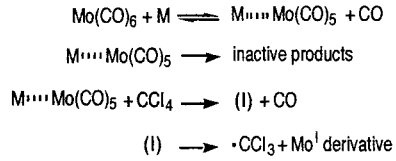


is still an effective co-initiator for hours after the light source is removed. This after-effect can be achieved with the addition of acetylacetone and will be identified as Z in Scheme 15A. Species **10** coordinated with acetylacetone reacts slowly with the halide and is believed to be responsible for the observed after-effect. On the other hand, the uncoordinated species **11** reacts rapidly with the halide and is responsible for the main source of initiation that occurs with the light source present. It should be noted that radical production still occurs without the addition of acetylacetone.

The thermal mechanism of radical formation with $Mn_2(CO)_{10}$/organohalide systems appears to be less understood. The thermal mechanism may occur by the homolytic scission of the Mn−Mn bond to create $Mn(CO)_5$ fragments that react with the organohalide since this mechanism is believed to also occur at lower temperatures upon photolysis as discussed previously.[105] However, Bamford conducted polymerizations with methyl methacrylate monomer initiated with $CCl_4/Mn_2(CO)_{10}$ in ethyl acetate at 80 °C,[106] which led to the proposed mechanism in Scheme 15B for thermal initiation with this system yielding carbon-based radicals. "Inactive products" are understood to be species or processes that are difficult to represent with specific structures that could be responsible for the deactivation of radical production leading to reduced rates of polymerization. The inactive products were necessary in explaining certain characteristics of the kinetic data.[102,106] Species **12** is taken as a reaction intermediate, and species **13** is taken as the side product of the reaction which forms the radical species. Although there have been conflicting mechanisms proposed for thermal initiation, both mechanisms suggest that manganese carbonyl fragments upon heating into a species that reacts with the halide such that a carbon-based radical is produced that is capable of initiating free radical polymerizations just as with photoinitiation.

$Mo(CO)_6$ has a relatively high thermal activity in the range of 70−80 °C for reacting with organohalides to produce carbon-centered radicals. Scheme 16 provides the thermal mechanism for radical formation using the $Mo(CO)_6/CCl_4$ co-initiator system. The first step involves a ligand exchange of CO from $Mo(CO)_6$ with some compound, most commonly monomer; however, solvents such as dioxane and ethyl acetate have been observed to behave similarly.[103] This now active, newly coordinated Mo species is believed to react with $CCl_4$ giving rise to the primary source of carbon-based free radicals during the early stages of the polymerization.[102] It should be noted that the monovalent Mo compound formed in the final reaction of Scheme 16 can undergo further oxidation to the pentavalent state, providing an additional source of radicals.[102,103]

**Scheme 16. Reaction Scheme Proposed for Radical Generation for the $Mo(CO)_6/CCl_4$ System under Thermal Conditions in the Presence of Monomer or Other Ligand Exchanging Species (M)[103]**



In regard to the halogenated species,[102,103] a wide variety of organohalides are capable of acting as co-initiators. Generally having halogens α to various allylic or carboxyl groups allows for a highly active site. Typically the replacement of Cl with Br or the addition of more halogens to a single carbon increases the reactivity of that particular site. Most of the halides used by Bamford were either trihalide substituents or carbon tetrachloride. Bamford suggests that graft copolymerizations are highly feasible with these types of systems and that since macroradicals are created specifically on the trunk polymer the production of homopolymer should result only from chain transfer.[103]

$Mn_2(CO)_{10}$ co-initiation has been used under thermal initiating conditions (80 °C) to synthesize poly(ethyl acrylate)−poly(styrene) and poly(methyl methacrylate)−poly(styrene) block copolymers.[107] The poly(ethyl acrylate) (DP = 242) and poly(methyl methacrylate) (DP = 312) starting backbones were synthesized such that a $CBr_3$ group terminated one chain end while the opposite end was capped with a Br group. The poly(styrene) portions of the block copolymers ranged in DPs of 50−670. Grafting of ultrafine silica, titanium oxide, and carbon black particles was performed with $Mo(CO)_6$ under thermal conditions where trichloro sites were introduced onto the particles by surface modifications with trichloroacetyl isocyanate.[108] Grafting yields of 740%, 150%, and 35% were achieved using methyl methacrylate on silica, titanium oxide, and carbon black particles, respectively. Styrene and *N*-vinylcarbazole monomers were grafted with yields ranging from 20% to 45% based on weight of particles charged.

## E. Assessment of Redox Initiating Methods

All of the redox systems discussed have the capability of generating radicals at specific sites when the

particular organic substrate (co-initiator 1), bonded to the trunk polymer, is permitted to react with the transition-metal species (co-initiator 2). By thus controlling the first step in a radical-based graft copolymerization, specific macroradical production is possible. However, due to their conventional nature, these systems are unable to control grafted chain molecular weight or minimize chain transfer of radicals from the growing grafted chain end. Having an appreciation of the redox-initiating chemistry is extremely important. Historically speaking, conducting a free radical graft copolymerization utilizing these redox techniques at lower temperatures and shorter reaction times accompanied with solvents and monomers with low chain transfer constants was probably the polymer chemist's greatest chance at minimizing homopolymerization.

Consequently, the following section will be devoted to living polymerization techniques and the benefits these systems offer with regard to molecular weight control and potential chain transfer reduction. The subsequent sections will then describe some of the free radical-initiating methods that have been recently developed and are not only capable of specific macroradical generation, but also yield extremely narrow molecular weight distributions. Many are capable of increasing molecular weight with monomer conversion in such a fashion that these systems behave in a more "living" manner when compared to conventional radical polymerizations. A significant reduction in the amount of homopolymer produced in a vinyl graft copolymerization appears more promising with these systems.

## VII. Radical Polymerization Methods which Exhibit Controlled/"Living" Character[109,110]

A polymer's molecular weight distribution can be measured by a quantity referred to as the polydispersity index (PDI) as shown in eq 22.

$$\mathrm{PDI} = \frac{\bar{M}_\mathrm{w}}{\bar{M}_\mathrm{n}} \tag{22}$$

The number average molecular weight ($\bar{M}_\mathrm{n}$) and the weight average molecular weight ($\bar{M}_\mathrm{w}$), are described in eqs 23 and 24, respectively

$$\bar{M}_\mathrm{n} = \frac{\sum N_\mathrm{i} M_\mathrm{i}}{\sum N_\mathrm{i}} \tag{23}$$

$$\bar{M}_\mathrm{w} = \sum w_\mathrm{i} M_\mathrm{i} = \frac{\sum N_\mathrm{i} M_\mathrm{i}^2}{\sum N_\mathrm{i} M_\mathrm{i}} \tag{24}$$

where $N_\mathrm{i}$ is the number of polymer molecules or moles of species i, $M_\mathrm{i}$ is the molecular weight of species i, and $w_\mathrm{i}$ is the weight fraction of species i in the entire polymer sample. In conventional free radical polymerization, PDIs in the range of 2−5, sometimes even higher, can be observed indicating there are many different species i in the sample (or a collection of molecules with a *dispersion* or range of molecular weights). Considering all of the radical-based reactions occurring, namely, initiation, propagation, termination by coupling and disproportionation (if it occurs to any noticeable extent), and chain transfer to reaction components, different molecular weight species are manifested due to the inherent complexity of the polymerization.

If a polymer sample was such that all of the species i were identical, meaning each had the same molecular weight, the PDI for the polymer equals one. Theoretically this monodisperse polymer could be synthesized if the nature of the polymerization is as follows: (1) every radical that will initiate the growth of a polymer chain is generated and initiates at the same time, (2) the propagation of each chain proceeds at a constant rate without the occurrence of chain transfer or premature termination of the active chain end, and (3) the polymerization is stopped in such a way that each chain is terminated in an identical manner at the same time. Polymerizations which follow the above scenario are impossible by conventional free radical methods; however, living chain growth polymerizations do provide a practical means toward synthesizing more monodisperse polymers.

A living chain growth polymerization is that in which the active propagating species participates in neither chain transfer nor termination reactions. One characteristic of a living system is that the concentration of active propagating species remains constant throughout the entire polymerization (to 100% monomer conversion), and if more monomer is added to the system, the polymerization can continue. A linear relationship is observed when molecular weight is plotted versus monomer conversion. Classically living chain growth polymerizations have been achieved with anionic, cationic, and ring-opening polymerizations. These systems typically operate from an equilibrium of active and dormant propagating species with the rate of polymerization described as shown in eq 25

$$R_\mathrm{p} = -\frac{\mathrm{d}[\mathrm{M}]}{\mathrm{d}t} = k_\mathrm{p}[\mathrm{M}^\bullet][\mathrm{M}] \tag{25}$$

where [M•] is the concentration of active propagating chain ends. Degrees of polymerization can be predicted as shown in eq 26

$$\bar{X}_\mathrm{n} = \frac{[\mathrm{M}]_\mathrm{o} - [\mathrm{M}]}{[\mathrm{I}]} \tag{26}$$

where $[\mathrm{M}]_\mathrm{o}$, [M], and [I] represent the original monomer concentration, the final monomer concentration, and initiator concentration, respectively. Polydispersity indices can be calculated by eq 27 for living chain growth polymerizations which approach monodispersity due to the reduction in the amount of chain transfer and termination reactions and especially if initiation is fast relative to propagation ($v$ is the fraction of monomer consumed).

$$\mathrm{PDI} = 1 + \frac{v}{(v+1)^2} \tag{27}$$

Equation 27 predicts that molecular weight distribu-

tions for living chain growth polymerizations will narrow as the degree of polymerization increases.[111]

Living polymerizations were normally confined to nonradical-based systems. However, with recent advances in polymer synthetic chemistry, methods of conducting radical-based polymerizations in a more "living" manner have been developed. Polymers obtained from these systems typically have lower polydispersity indices (many with $1 < PDI < 1.5$), suggesting that the termination and chain transfer reactions are not occurring to the extent that is observed in conventional free radical polymerizations. Moreover, the lower PDIs allow the formation of uniform architectures, simplifying the subsequent understanding of structure−property relationships. The advantages of living techniques in regard to designing more complex macromolecular architectures have been outlined by Webster,[112] thus making the development of "living" or controlled radical polymerization techniques an extremely important synthetic tool due to the greater versatility of the radical mechanism.

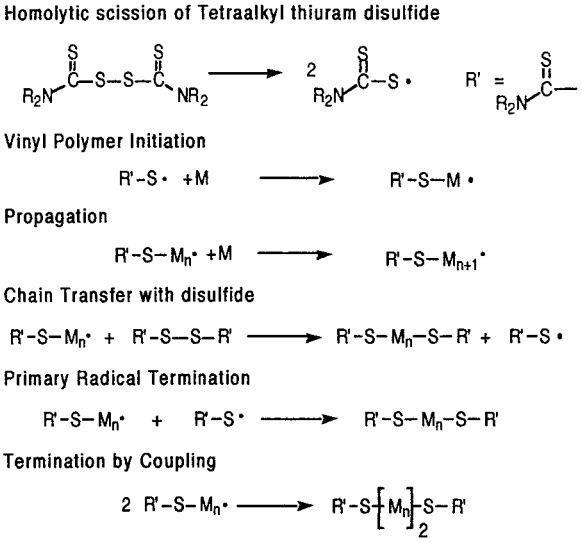
Before specific methods are discussed, the term "living" for these radical systems needs to be qualified. The mechanism for an ideal living polymerization is one where chain transfer and termination reactions are absent. The various examples discussed below are more correctly referred to as controlled or "living" processes due to the fact that transfer and termination are more controlled relative to conventional radical polymerizations; however, these chain-breaking reactions are noticeable when synthesizing higher molecular weight polymers.

Under normal conditions, bimolecular termination is reduced as a result of the lower radical concentrations and chain transfer can be greatly reduced as indicated by low PDIs. However, suppressing these chain-breaking reactions is accomplished by limiting the degrees of polymerization. For example, to reduce the effects of chain transfer to monomer, the desired DPs should remain below those shown in eq 28.[113]

$$DP = \frac{[M]_o - [M]}{[I]_o} < \frac{0.1k_p}{k_{tr,M}} \qquad (28)$$

Equation 28 is based on the fact that suppressing chain transfer to monomer relative to propagation will not be affected by reducing radical concentrations since both reactions are first order with regard to the radical chain end concentration. Having an equilibrium between active and dormant chain ends (the key to the livingness of these systems), the addition of monomer is slowed due to the lower concentration of radicals present relative to the concentration that could exist if radical generation were not reversible. Lower radical concentrations have a tremendous effect on lowering the rate of termination since this reaction is second order with regard to the radical chain end concentration. By establishing a molecular weight threshold simply by choosing the proper ratio of monomer to initiator, polymerizations can be conducted in such a manner that the likelihood of both transfer and termination are extremely low. It should be noted that these systems do not change the inherent reactivity of the radical toward propagation, termination, or transfer. It simply slows the polymerization and helps to control the kinetic chain length so that polymers can be synthesized in a controlled manner and stopped (by reaching high conversions) before transfer and/or bimolecular termination are experimentally noticeable.

**Scheme 17. Structure of Tetraalkyl Thiuram Disulfide and Its Function in a Vinyl Polymerization[118]**

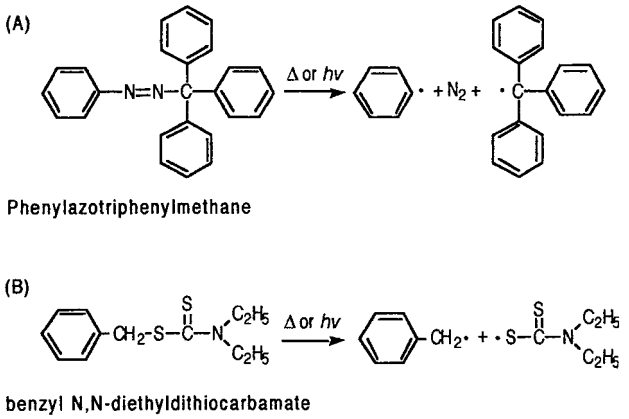



The intent of this article is not to provide an exhaustive review of controlled radical polymerizations but rather to provide several examples of systems which either are highly prominent in the literature (Iniferters, Nitroxides, ATRP) or are more recent developments in the field (RAFT). For example, important contributions such as from Wayland's group,[114] where organocobalt porphyrin complexes were used to control acrylate polymerizations, are not discussed here. For a more comprehensive review, especially in regard to the history of controlled radical polymerizations, *ACS Symposium Series 685* should be consulted.[115]

## A. Iniferters

An advance toward obtaining a more controlled radical polymerization was developed by Otsu and Yoshida[116] with the "iniferter" concept. Work in this area has been reviewed by Otsu and Matsumoto[117] and by Reghunadhan and Clouet.[118] An iniferter is defined as a species that can act as an *ini*tiator, chain trans*fer* agent, and *ter*minator. The first type of iniferters used were those of tetralkyl thiuram disulfide, whose structure and roles in a polymerization (acting as initiator, chain transfer agent, and primary radical terminator) are shown in Scheme 17. The disulfide iniferter, being activated thermally or with light, generates symmetric species through homolytic scission of the S−S bond that participate in the reactions shown in Scheme 17. Iniferters provided not only a means of having more control over the chain end functionality, but also it was observed that the *S*-alkyl dithiocarbamate moiety participated in a reversible photodissociation,[116] permitting the syn-

**Scheme 18. Radical Generation by Thermal Activation or Photoactivation of Phenylazotriphenylmethane (A) and Benzyl *N,N*-Diethyldithiocarbamate (B)[117]**

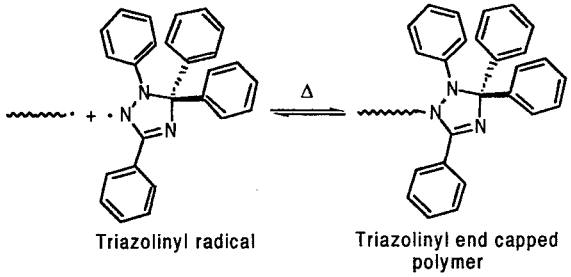



thesis of block copolymers in the presence of a vinyl monomer with a macroinitiator having an *S*-alkyl dithiocarbamate chain end.

Other types of iniferters, namely, phenylazotriphenylmethane, can be thermally or photolytically activated where the bond dissociation generates two dissimilar species as indicated in Scheme 18A. The radical species generated with this iniferter are a reactive phenyl radical that is believed to initiate the vinyl polymerization accompanied by a triphenylmethyl radical that is relatively stable (not able to promote initiation). However, this triphenylmethyl radical does reversibly react with the propagating polymer chain radical, a feature which provides better control over the polymerization. The mechanism is believed to begin by the phenyl radical initiating the polymerization. The polymer chain continues to propagate in the presence of monomer until the triphenylmethyl radical caps the chain end yielding a dormant chain. The chain end can undergo a reversible homolytic cleavage, generating the active radical chain end, free to propagate, and the stable triphenylmethyl radical as long as heat or light are available. Generally iniferters that dissociate into two different radicals, one being much more reactive than the other (in terms of initiating a polymerization), appear to provide better control over vinyl polymerizations. For example, polymerizations with methyl methacrylate using the phenylazotriphenylmethane iniferter can be conducted where both monomer conversion and $\bar{M}_n$ increase linearly with time. Although the polymerization exhibited a more controlled character in regard to $\bar{M}_n$ development, PDIs ranged from 2 to 5.[119]

Styrene polymerizations can have similar linear increases of monomer conversion and $\bar{M}_n$ with time when conducted with the benzyl *N,N*-diethyldithiocarbamate (BDC) iniferter, whose mechanism for radical formation is shown in Scheme 18B. The benzyl radical is believed to be the more active radical responsible for initiation, while the less reactive dithiocarbamate radical provides a certain degree of control by its participation in the reversible activation and deactivation of the propagating chain end. Polydispersity indices for polystyrenes generated in this manner have been on the order of 2−3,[120] indicating that the polymerization does not completely satisfy the strict criteria for a living polymerization. Otsu et al.[121] note that when using the BDC iniferter, the dithiocarbamate radical can function as both an initiator (Scheme 17) and a polymer chain terminator, leading to a more complicated mechanism that decreases the chances of obtaining narrow molecular weight distributions. However, BDC moieties have controlled the synthesis of low molecular weight poly(methyl methacrylate) ($\bar{M}_n \approx 555-1020$) with PDIs ranging from 1.2 to 1.07.[122] Excellent control (micrometer order precision) over the patterning of biomedical surfaces functionalized with BDC groups has been possible where portions of these surfaces were selectively photografted with different water-soluble vinyl monomers.[123]

**Scheme 19. Thermal Reversible Capping of a Propagating Polymer Chain Using Triazolinyl Radicals[124]**




Triazolinyl radicals have been used to reversibly end cap propagating radicals (Scheme 19) to conduct more controlled polymerizations of styrene.[124] The integrated form of eq 25 is shown in eq 29

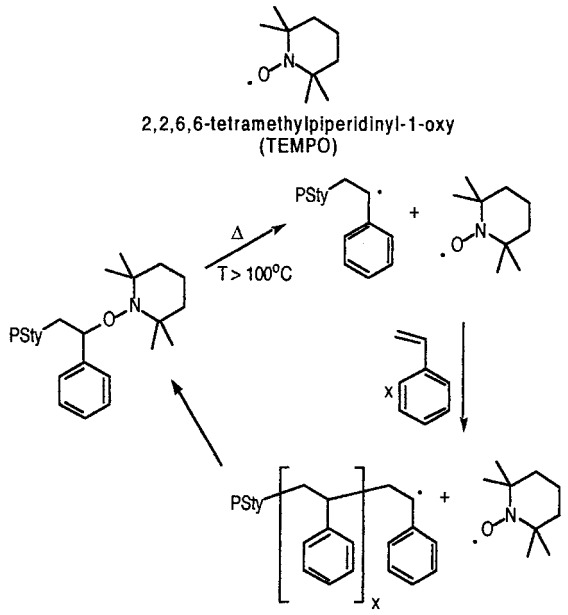
$$\ln\left(\frac{[M]_o}{[M]}\right) = k_{app}t \qquad (29)$$

where $[M]_o$ is the initial monomer concentration, [M] is the monomer concentration at time $t$, and $k_{app} = k_p[M^\bullet]$. Using this system for bulk styrene polymerizations, linear plots of $\ln([M]_o/[M])$ versus time were obtained indicating a constant concentration of propagating centers throughout the entire polymerization. $\bar{M}_n$ increased linearly with monomer conversion, and polystyrene with a $\bar{M}_n$ of 20 700 was reported to have a PDI of 1.86. Although improvements have been made in controlling vinyl polymerizations using iniferters (especially with end group functionalization), much greater control is available with use of the various polymerization techniques to be discussed in the following sections.

## B. Nitroxides[115,117,125]

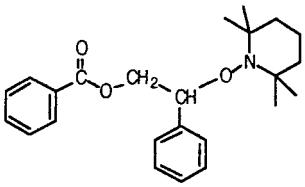
Beginning with the work of Moad et al.[126] and Georges et al.,[127] various nitroxides have been utilized in recent years to promote control over radical-based polymerizations, the most prominent being 2,2,6,6-tetramethylpiperidinyl-1-oxy (TEMPO). Originally styrene and various styrene derivatives were the major types of monomers to be successfully polymerized in a controlled manner with this system; however, success with other types of monomers is

**Scheme 20. Reaction Scheme for the Thermal Radical Polymerization of Styrene Controlled by TEMPO[125]**




increasing. The control is believed to occur from an equilibrium between active and dormant chain ends as shown in Scheme 20. A dormant chain is one where the TEMPO moiety is covalently attached to the polystyrene chain end by means of a C−O bond. With the application of heat, the C−O bond undergoes homolytic scission to form an active polystyrene chain end and a stable TEMPO radical. The TEMPO radical is not believed to initiate the vinyl polymerization of styrene monomer. The active chain end is now capable of increasing its molecular weight by the addition of monomer. At some point in time, the TEMPO radical caps the growing chain end by forming a C−O linkage, recreating the dormant polymer chain. This reversible termination mechanism repeats itself during the course of the polymerization and is capable of producing polystyrene with PDIs in the range of 1.1−1.3.[125] Since dormant chains are present throughout the polymerization, radical concentrations are reduced making bimolecular termination reactions between polymer chain ends less likely. Other reactions that occur at the high temperatures used are the self-initiated polymerization of styrene and the decomposition of the nitroxide moiety, most likely by means of $\beta$-H abstraction of polymer chain end groups by nitroxyl radicals yielding an unsaturated polymer chain end group and a hydroxylamine.

Originally these polymerizations were initiated by heating bimolecular initiators such as benzoyl peroxide in bulk styrene in the presence of TEMPO. However, in terms of chain architecture and molecular weight, better control has been achieved with compounds such as **14**[128] and **15**. The use of unimolecular initiators has allowed control over the molecular weight by varying the monomer-to-initiator ratio. With the homolytic dissociation of **14** and **15** at the C−O bond, an active substituted benzylic radical is created that is capable of reacting with styrene monomer to initiate the polymerization. As



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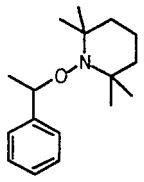

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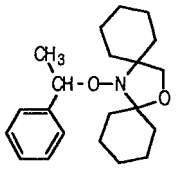
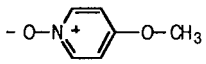
a consequence of the simultaneous formation of the TEMPO radical from the homolytic C−O cleavage, the overall mechanism is fundamentally the same as that illustrated in Scheme 20. Experimental molecular weights match extremely well with those theoretically predicted by the monomer to unimolecular initiator ratio up to molecular weights of ~30 000−50 000. Above 50 000, the experimental molecular weights are lower than those predicted as a consequence of self-initiated polymerization.[125]

Recent work has yielded other nitroxide compounds capable of mediating vinyl polymerizations in a controlled manner. The use of unimolecular initiator **16** in the bulk polymerization of styrene at 110 °C yielded polymers with PDIs on the order of 1.5, even at 90% monomer conversion.[129] Linear plots of ln-



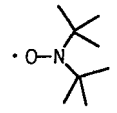
16

($[M]_o/[M]$) versus time were obtained up through 80 h of reaction time, and $\bar{M}_n$ increased linearly with monomer conversion. Methyl methacrylate polymerizations initiated by a cumyl hydroperoxide/ferrous-(II) sulfate redox system have been performed in the presence of 4-methoxypyridine *N*-oxide **17**.[130] Poly-



17

merizations conducted in a 1/1 (v/v) water/acetonitrile mixture at 50 °C provided linear increases in $\bar{M}_n$ up to 25% monomer conversion with PDIs in the range of 1.2−1.3, and excellent agreement was observed between experimental and theoretical molecular weights up to $\bar{M}_n$ of 35 000. It should be noted that **17** is not initially the oxygen-based radical necessary for controlling the polymerization. Little mechanistic detail is known in regard to how **17** is oxidized. It is speculated that the Fe(III) species produced from the peroxide/Fe(II) initiating system, a type of Fenton's reagent, could serve to oxidize **17**, yielding the radical derivative of **17** and Fe(II). Radical polymerizations of *tert*-butyl acrylate (tBA) have been mediated with di-*tert*-butyl nitroxide (DBN) **18**, yielding $\bar{M}_n$ and PDIs of 4000−6000 and 1.3−1.4, respectively.[131] An interesting characteristic of this polymerization is that the PtBA−DBN adduct was observed to decompose at 4 times the rate known for decomposition observed in TEMPO-mediated polystyrene polymerizations. This decomposition occurs by $\beta$-H abstrac-



18

tion of PtBA end groups with **18** to yield an unsaturated PtBA end group and hydroxylamine.

The kinetics of nitroxide-mediated styrene polymerizations have been studied[132−134] and are based on understanding the equilibrium that develops between the active and dormant species as shown below in eq 30

$$P^{\bullet} + N^{\bullet} \underset{k_d}{\overset{k_c}{\rightleftharpoons}} P-N \qquad (30)$$

where P• represents the propagating radical and N• represents the nitroxyl radical. The change in propagating and nitroxyl radical concentrations with respect to time can be described by eqs 31 and 32, respectively.

$$\frac{d[P^{\bullet}]}{dt} = R_i - k_t[P^{\bullet}]^2 + k_d[P-N] - k_c[P^{\bullet}][N^{\bullet}] \qquad (31)$$

$$\frac{d[N^{\bullet}]}{dt} = k_d[P-N] - k_c[P^{\bullet}][N^{\bullet}] \qquad (32)$$

Without an excess of nitroxyl radicals added to the polymerization, a steady state of propagating and nitroxyl radical concentrations exists during the initial stages of the polymerization, thus setting eqs 31 and 32 equal to zero. Defining $K = k_d/k_c$ then the concentration of propagating and nitroxyl radicals can be represented as shown in eqs 33 and 34.

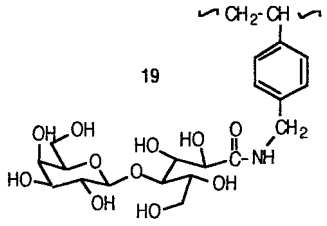
$$[P^{\bullet}] = \left(\frac{R_i}{k_t}\right)^{1/2} \qquad (33)$$

$$[N^{\bullet}] = \frac{K[P-N]}{[P^{\bullet}]} \qquad (34)$$

Substituting eq 33 into eq 25, the rate of polymerization can be represented as

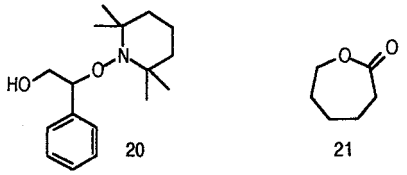
$$R_p = \left(\frac{k_p^{\,2} R_i}{k_t}\right)^{1/2} [M] \qquad (35)$$

Equation 35 indicates that the rate of polymerization is independent of the nitroxide or P−N concentration. Ohno et al.[135] showed that the rate of radical polymerizations of *p-tert*-butoxystyrene monomer mediated by TEMPO are also independent of the TEMPO concentration. The polymerizations exhibited a living nature in that $\bar{M}_n$ increased linearly with conversion, yielding polymers with $\bar{M}_n$ and PDI on the order of 60 000 and 1.2, respectively. Copolymers of styrene and *N*-vinyl carbazole (1:1 monomer ratio) have been formed in the presence of TEMPO to yield $\bar{M}_w$ on the order of 4000 with a PDI of 1.15 where 20% of the polymer was comprised of *N*-vinyl carbazole repeat units.[136] Glycopolymers, namely, well-defined polymer (PDI ≈ 1.1) with repeat structure **19**, have also been synthesized in a controlled manner by mediation with **18**, yielding molecular weights in the range of 2000−40 000.[137]

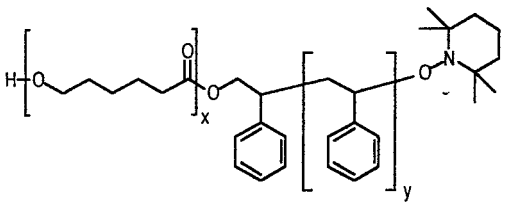


19

Block copolymers have been synthesized with ϵ-caprolactone and styrene which polymerize by fundamentally different chain growth mechanisms: ring opening and radical, respectively.[138] The synthesis was performed by using a dual initiator **20**. The hydroxyl group of **20**, accompanied with $Al(OiPr)_3$, served as the initiating site for the ring-opening polymerization of ϵ-caprolactone **21**, while the TEMPO moiety controlled the radical polymerization of styrene. Block copolymers **22** were synthesized with overall $\bar{M}_n$ ranging from 17 500−149 000 with PDIs in the range of 1.07−1.41.

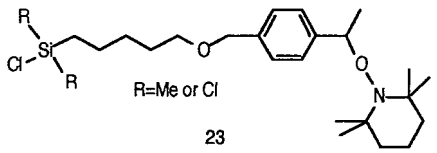


20 21



22

TEMPO moieties have been bonded to the surface of silica particles through Si−O linkages by reacting the Si−Cl group of **23** with surface hydroxyl groups.[139]



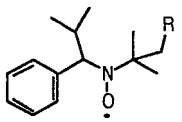
R=Me or Cl

23

Polystyrene chains could be grafted with $\bar{M}_n$ of 51 000 and PDIs of 1.14. Low TEMPO concentrations on the silica particles resulted in a lack of control over the polymerization when conducted at high monomer concentrations. Efforts to reduce styrene concentrations in hopes of gaining control greatly reduced polymerization rates. Alkoxyamine **15** was added to promote better control over the polymerization at high monomer concentration while operating under reasonable polymerization rates. However, homopolymer was produced (added **15** was not attached to the silica) as a result and had to be extracted from the silica particles. The addition of TEMPO rather than **15** possibly could have controlled the polymerization without producing as much homopolymer, although

this would still not prevent homopolymer if self-initiation of styrene was significant. The addition of compounds such as benzoyl chloride or acetic anhydride has been found to reduce the amount of styrene self-initiation.[125] Interestingly, nitroxides have also aided in the production of uniform gels. Polystyrene gels have been synthesized by copolymerizing styrene with small amounts (<3 mol %) of 4,4′-divinylbiphenyl, where the process was controlled by TEMPO.[140] The gels produced had a remarkably uniform cross-linking density with no observable microgel formation due to the high degree of control exhibited by TEMPO mediation.

Generally controlling radical polymerizations with nitroxide radicals has been shown to be an extremely useful tool for synthesizing polymers with low polydispersity indices (PDI < 1.3). Although the use of nitroxides has mainly been used for controlling styrene polymerizations, recent work devoted to synthesizing different types of unimolecular nitroxide initiators[141,142] could eventually lead to better control over an even wider range of monomers. For example, Benoit et al.[142] successfully controlled polymerizations of acrylate-, acrylamide-, acrylonitrile-, and styrene-based monomers using **24**-based compounds where molecular weights ranged from 1000 to 200 000 with PDIs on the order of 1.05−1.15.

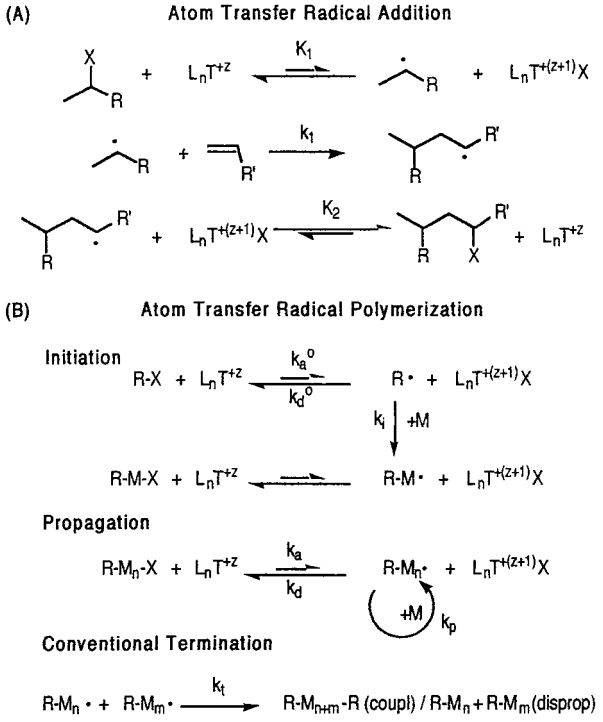


24

## C. Atom Transfer Radical Polymerization (ATRP)[115,143,144]

Atom transfer radical polymerization (ATRP) is another "living" technique which provides considerable control over radical polymerizations with common vinyl monomers. ATRP is an extension of atom transfer radical addition (ATRA) or more generally the Kharasch addition reaction.[145] ATRA is a method of adding halogenated alkanes to alkenes through a radical-based mechanism which can be catalyzed with various metal complexes. Scheme 21A provides the general mechanism of ATRA. The metal complex (reductant) reacts with the organohalide (oxidant) via a redox mechanism, creating a carbon-centered radical while increasing the valence state of the metal complex by one. The C−X bond of the organohalide is broken, leaving a radical at the carbon while the halogen gains the electron creating a halide which is subsequently included in the metal complex. The carbon-centered radical subsequently reacts with the alkene in the same manner as a conventional radical initiator reacts with a vinyl monomer yielding a new carbon-centered radical. The addition reaction is completed by the metal complex, in its higher valence state, undergoing a reverse redox reaction where the halogen atom caps the radical, generating a new carbon−halogen bond and returning the metal complex to its original valence state. It should be noted that the creation and capping of radicals through the redox reactions are considered to be reversible processes; however, the reverse reaction (radical capping) is more highly favored.

**Scheme 21. General Mechanism for ATRA (A) and ATRP (B)**[a]

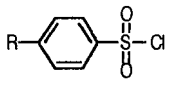



[a] $L_nT$ = metal complex at a certain valence state $z$, X = halogen (Cl or Br), and M = Monomer.[143]

ATRP is a modification of ATRA in the sense that multiple alkenes (vinyl monomers) are added (propagated) to the radical in a chain growth mechanism giving rise to a polymer chain. The creation and capping of radicals at the polymer chain end proceed in the same manner as that of ATRA. The general reaction scheme for ATRP is provided in Scheme 21B. The "living" mechanism exhibited by ATRP in many ways is analogous to that understood with nitroxide mediation, namely, an equilibrium is established between active and dormant chains (dormant being the more prevalent of the two) allowing monomer addition to the polymer chain end in a controlled manner. It should be noted that $k_d \gg k_p$ in order to have substantial control over the polymerization. "Living" characteristics of ATRP are exhibited in that linear plots of $\ln([M]_o/[M])$ versus time and molecular weight versus monomer conversion can be obtained. Normally initiation is relatively fast, and in conjunction with the "living" nature of the polymerizations, extremely narrow PDIs, as low as 1.05, have been reported.

Various types of organohalides can be used as co-initiators for ATRP.[115,143,144] Chloro and bromo compounds have been the most successful in terms of molecular weight control. Generally the same types of activated halogenated sites which are useful co-initiators with metal carbonyls (section VI. D.) are capable of co-initiation in ATRP. Alkyl halides perform well when their structures resemble those of the halogenated polymer chain end. For example, styrene polymerizations often incorporate 1-phenylethyl chlorides or bromides as the initiators. An interesting

class of co-initiators is that of arenesulfonyl halides **25**.[146] Due to the relatively poor conjugation of the

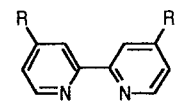


R= $CH_3$, $CH_3O$, F, or H

25

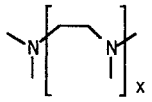
sulfonyl radical with the phenyl ring, the type of para substituent incorporated is of little importance in regard to successful initiation and control. Thus, all variations of **25** have been useful initiators for controlled polymerizations of styrene and methyl methacrylate. Generally these compounds exhibit relatively fast initiation which is necessary for the synthesis of polymers with low dispersities.

Several metal complexes, comprised of Cu(I), Fe(II), Ni(II), and Ru(II), have been successfully used as catalysts for ATRP.[147] For example, $RuCl_2(PPh_3)_3$ in the presence of $Al(OiPr)_3$ can provide excellent control of methyl methacrylate polymerizations (PDI $\approx$ 1.1). However, the most widely used class of metal complexes are copper based. The Cu(I) ion can be complexed with a wide variety of ligands, most commonly nitrogen based, such as bipyridine derivatives **26**,[148,149] and multidentate amine ligands **27**,[150] as well as tris[2-(dimethylamino)ethyl]amine ($Me_6$-TREN) **28**.[151] Typically metal complexes are such that



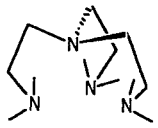
R = H, n-heptyl, or 5-nonyl

26



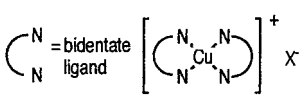
x = 1, 2, or 3

27



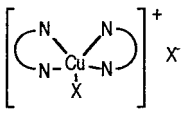
28

four nitrogens are complexed with the Cu atom. For example, the positioning of bidentate ligands such as **26** or **27** ($x = 1$) around the copper atom, Cu(I), are envisioned as shown in **29**. When the copper complex has reacted with the organohalide site, structure **29** is oxidized to the Cu(II) state where the halide ($X^-$) is believed to be incorporated in the complex as shown in **30**. It should be noted that **29** and **30** are



= bidentate ligand

29



30

most likely oversimplified versions of the metal complex's true geometry, and thus, variations of this arrangement could exist depending on the experimental conditions, namely, the solvent and the actual ligands involved.[115]

Monomers having the most success in ATRP are styrenes, methacrylates, acrylates, and acrylonitrile. Polymerizations of acrylic and methacrylic acids have been unsuccessful because the carboxylic acid side groups react with the metal complexes creating metal carboxylates which are ineffective catalysts for ATRP. Ethylene, vinyl chloride, and vinyl acetate polymerizations have been difficult to control with ATRP due to the more highly reactive propagating radicals characteristic of these monomers. Typically ATRP is performed in bulk monomer; however, nonpolar solvents (*p*-xylene, *p*-dimethoxybenzene, and diphenyl ether) and polar solvents (ethylene carbonate and propylene carbonate) have been utilized as diluents for ATRP.[115,143,144] Aqueous-based polymerizations have been conducted in a controlled manner with monomers such as sodium methacrylate,[152] monomethoxy-capped oligo(ethylene oxide) methacrylate,[153] ammonium 2-sulfatoethyl methacrylate, sodium 4-vinylbenzoate, and vinylbenzyltrimethylammonium chloride.[154]

Efforts to investigate the kinetics of ATRP have focused on copper-based systems under homogeneous conditions. The general approach has been to experimentally determine reactant orders based on rate laws derived from Scheme 21B, which will be outlined in the discussion below, where $M-X = R-M_n-X$, $M^\bullet = R-M_n^\bullet$, and Cu(I) and Cu(II) represent metal complexes $L_nT^{z+}$ and $L_nT^{(z+1)+}X$, respectively. Assuming a steady-state concentration of polymer chain radicals, $M^\bullet$, the change in $[M^\bullet]$ with respect to time can be described by eq 36

$$\frac{d[M^\bullet]}{dt} = k_a[M - X][Cu(I)] - k_d[M^\bullet][Cu(II)] = 0 \quad (36)$$

which can subsequently be rearranged to

$$[M^\bullet] = \frac{k_a[M - X][Cu(I)]}{k_d[Cu(II)]} \quad (37)$$

Substituting eq 37 into eq 25, the rate of ATRP can be described as

$$R_p = -\frac{d[M]}{dt} = k_p[M^\bullet][M] = k_p[M]\left(\frac{k_a[M - X][Cu(I)]}{k_d[Cu(II)]}\right) \quad (38)$$

An interesting aspect of the rate expression, eq 38, is that it includes a term for the oxidized metal catalysts, Cu(II). Without any added Cu(II) complex, the initial Cu(II) concentration is zero. As the metal complex Cu(I) reacts with the organohalide, the radical and Cu(II) concentrations increase to equal values on the order of $10^{-5}$ mol/L. Because of the persistent radical effect,[155] the highly reactive propagating radicals undergo bimolecular termination to a certain extent until a radical concentration of $\sim 10^{-7}$ mol/L is obtained. The Cu(II) concentration is now 2−3 orders of magnitude higher than the radical concentration, allowing a controlled process. Electron paramagnetic resonance (EPR) studies have been conducted with copper-mediated ATRP to investigate Cu(II) concentrations. From these studies, the amount of charged Cu(I) which is oxidized to the Cu(II) species in styrene,[156] methyl methacrylate, and methyl acrylate[157] polymerizations is approximately 4−6%, 5−6%, and 3%, respectively. The extent of premature bimolecular termination can be reduced with the addition of $\sim$5 mol % of the Cu(II) complex (relative

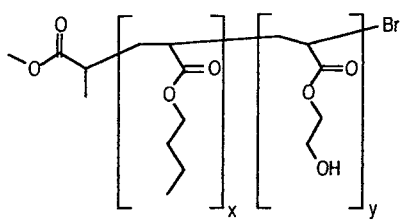
**Table 5. Molecular Weight Data for Various Vinyl Monomers Polymerized Using Different ATRP Systems[a]**

| organohalide (R−X) | metal complex ($L_nT^{z+}$) | monomer | $\bar{M}_n$ | PDI |
|---|---|---|---|---|
| 2-bromoethyl isobutyrate[b] | $Ni\{C_6H_3(CH_2NMe_2)_2\}Br$ | MMA | 28 000 | 1.10 |
| $CCl_4$c | $RhCl(PPh_3)_3$ | MMA | 28 500 | 1.48 |
| $PhCOCHCl_2$d | $RuCl_2(PPh_3)_3/Al(OiPr)_3$ | MMA | ∼10 000 | 1.11 |
| $CCl_3Br$ | $NiBr_2(PPh_3)_3/Al(OiPr)_3$ | MMA | 11 700 | 1.20 |
| $CH_3CBr(CO_2Et)_2$f | $FeCl_2(PPh_3)_3$ | MMA | 12 000 | 1.29 |
| *p*-toluenesulfonyl chloride[g] | $FeBr_2$/dNbipy | MMA | 75 000 | 1.24 |
| $Ph_2CHCl$[h] | CuCl/dNbipy | MMA | 18 000 | 1.05 |
| methyl 2-bromopropionate[i] | CuBr/bipy | HEA | 16 000 | 1.20 |
| methyl 2-bromopropionate[j] | CuBr/dNbipy | GA | 53 000 | 1.20 |
| α,α′-dibromoxylene[k] | CuBr/bipy | 4-AcOSt | 7 500 | 1.20 |
| *p*-toluenesulfonyl chloride[l] | CuBr/dNbipy | MMA | 20 000 | 1.10 |
| α,α′-dibromoxylene[148] | CuBr/bipy | St | 12 000 | 1.12 |
| methyl 2-bromopropionate[148] | CuBr/bipy | MA | 29 000 | 1.15 |
| 1-phenylethyl bromide[m] | CuBr/bipy | 3-$CF_3$St | 12 000 | 1.20 |

[a] MMA = methyl methacrylate, dNbipy = 4,4′-bis(5-nonyl)-2,2′-bipyridine, bipy = 2,2′-bipyridine, HEA = 2-hydroxyethyl acrylate, GA = glycidyl acrylate, 4-AcOSt = 4-acetoxystyrene, St = styrene, MA = methyl acrylate, 3-$CF_3$St = 3-$CF_3$ styrene. [b] Granel, C.; Dubois, P.; Jérôme, R.; Teyssié, P. *Macromolecules* **1996**, *29*, 8576. [c] Moineau, G.; Granel, C.; Dubois, P.; Jérôme, R.; Teyssié, P. *Macromolecules* **1998**, *31*, 542. [d] Nishikawa, T.; Ando, T.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **1997**, *30*, 2244. [e] Uegaki, H.; Kotani, Y.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **1997**, *30*, 2249. [f] Ando, T.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **1997**, *30*, 4507. [g] Matyjaszewski, K.; Wei, M.; Xia, J.; McDermott, N. E. *Macromolecules* **1997**, *30*, 8161. [h] Wang, J.-L.; Grimaud, T.; Matyjaszewski, K. *Macromolecules* **1997**, *30*, 6507. [i] Coca, S.; Jasieczek, C. B.; Beers, K. L.; Matyjaszewski, K. *J. Polym. Sci., Polym. Chem. Ed.* **1998**, *36*, 1417. [j] Matyjaszewski, K.; Coca, S.; Jasieczek, C. B. *Macromol. Chem. Phys.* **1997**, *198*, 4011. [k] Gao, B.; Chen, X.; Iván, B.; Kops, J.; Batsberg, W. *Macromol. Rapid Commun.* **1997**, *18*, 1095. [l] Grimaud, T.; Matyjaszewski, K. *Macromolecules* **1997**, *30*, 2216. [m] Qiu, J.; Matyjaszewski, K. *Macromolecules* **1997**, *30*, 5643.

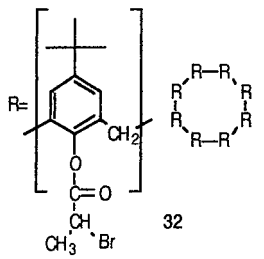
to the Cu(I) complex) before the polymerization is begun. In regard to the rate law for ATRP provided in eq 38, kinetic studies of styrene[149] and methyl methacrylate[158] found reactant orders for monomer, organohalide (M−X), and Cu(I) to be unity. Determining the order of Cu(II) was complicated by the persistent radical effect. Work with methyl acrylate did however find an inverse first-order dependence for the Cu(II) concentration, but reactant orders for monomer and Cu(I) were difficult to determine. A reactant order of 0.8 was found for the organohalide initiator (M−X).[159]

Table 5 provides molecular weight data for a wide variety of vinyl monomers polymerized using different types of ATRP systems. ATRP has proven to be a relatively versatile system providing excellent control over radical-based polymerizations with PDIs for the different polymers ranging from 1.05 to 1.48 (mostly 1.20 or lower). Besides homopolymer synthesis, various types of copolymers have been synthesized using ATRP. Amphiphilic block copolymers **31** have been synthesized using methyl 2-bromopropionate and CuBr/**27** ($x = 2$) initiation by successive addition of monomers (homopolymers with one monomer were synthesized such that the halogenated end group was used as a macroinitiator for polymerizing the second monomer).[160] Block copolymers **31** having




**31**

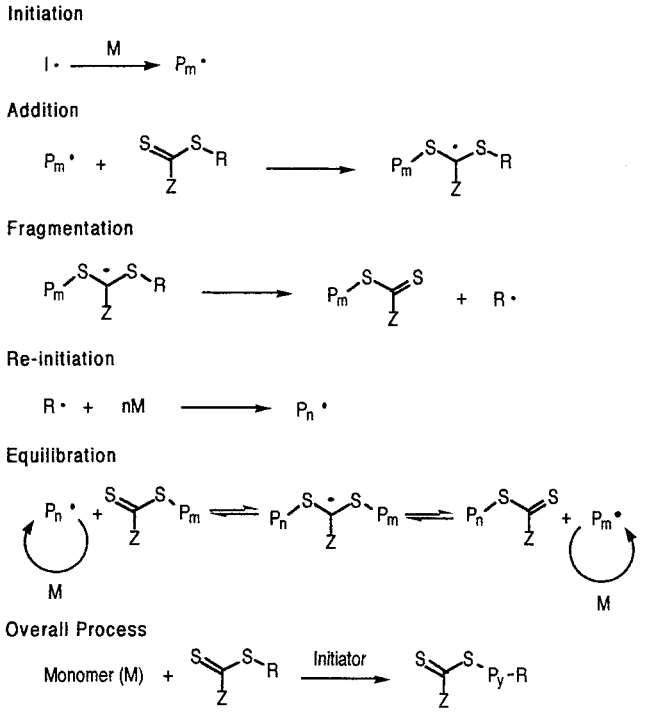
50:50 monomer compositions were obtained with overall $\bar{M}_n$ and PDI of 12 300 and 1.19, respectively. A−B−A triblock copolymers of styrene and 4-acetoxystyrene were synthesized using a α,α′-dibromoxylene/CuBr/bipy ATRP system, where overall block copolymer molecular weights of 21 000−25 000 having PDIs of 1.15 were synthesized.[161] Other types of block copolymers have combined ring-opening mechanisms with radical mechanisms.[162,163] For example, tetrahydrofuran was cationically polymerized with a ring-opening mechanism where the cationic site grew from one end of the polymer chain while having a Br moiety attached at the opposite end. With this poly(THF) macroinitiator, methyl acrylate, methyl methacrylate, and styrene monomers were block copolymerized where overall block copolymer molecular weights of 20 000−30 000 were synthesized with PDIs ranging from 1.2 to 1.5.[163] Polystyrene stars have been synthesized using an octafunctional organohalide **32** with CuBr/bipy.[164]




**32**

Octafunctional stars could be synthesized having narrow PDI (∼1.2) with overall molecular weights as high as 340 000. Brominated ethylene−propylene−diene terpolymer (EPDM-Br) was grafted at 90 °C for 20 h with methyl methacrylate with 93% efficiency (of polymer formed, 93% was grafted) where the ratio of EPDM-Br:CuBr:bipy was 1:0.8:2.4.[165] Other examples demonstrating the versatility of ATRP include the synthesis of architectures such as dendrimer-like star block copolymers,[166] polystyrene[167] and poly(methyl methacrylate)[168] labeled with anthracene, and various hyperbranched polymers.[169−172]

**Scheme 22. General Mechanism for Controlled Radical Polymerization of Vinyl Monomer M with the RAFT Technique[176,177]**




Controlling a radical polymerization with ATRP does not necessarily have to involve co-initiation with an organohalide. Reverse ATRP[173,174] has been performed with several different monomers, namely, styrene, methyl acrylate, and methyl methacrylate. A controlled radical polymerization can occur when initiators such as AIBN are heated in the presence of $CuCl_2$ complexed with either dNbipy or bipy, **26**. The radicals created by the decomposition of AIBN initiate the growth of a polymer chain, but the polymerization becomes controlled in the presence of the copper complex, $L_nT^{(z+1)+}X$ with the same mechanism as shown in Scheme 21B. Depending on the conditions, molecular weights on the order of 16 000−28 000 were synthesized with PDIs ranging from 1.1 to 1.4.

Generally ATRP is a versatile technique capable of controlling radical polymerizations to yield various vinyl polymers with extremely low PDIs (<1.20). Well-defined copolymer architectures, for example, block and star types, have also been successfully synthesized with ATRP methods.

## D. Reversible Addition-Fragmentation Chain Transfer (RAFT)

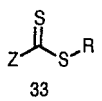
The RAFT technique incorporates a degenerative chain transfer mechanism to establish an equilibrium between active and dormant chain ends that promotes a controlled/"living" radical polymerization of common vinyl monomers.[175] Chiefari et al. were the first to report RAFT-controlled polymerization using various dithioesters as the chain transfer agent.[176] Scheme 22 provides the general mechanism involved in RAFT polymerization. Typical radical initiators such as azobisisobutyronitrile or benzoyl peroxide are added to start the growth of polymer chains which subsequently react with the dithioester, producing a dormant chain end (capped with the dithioester moiety) and a radical species, R•, that initiates the growth of a new polymer chain. Once the proper concentrations of propagating polymer chains and dormant chains are obtained, an equilibrium is developed where the dithioester group is transferred reversibly between different polymer chain ends, creating the necessary balance of active and dormant chains for a controlled process. The "living" nature of RAFT has been demonstrated with methyl methacrylate polymerizations where linear increases in $\bar{M}_n$ and decreases in PDI with monomer conversion were observed.[176]

**Table 6. Molecular Weight and Conversions of Various Monomers Polymerized Using the RAFT Mechanism Conducted with Different Dithioesters and Initiators[a]**

| monomer | dithioester | initiator | % conversion | $\bar{M}_n$ | PDI |
|---|---|---|---|---|---|
| MMA[176] | 34 | AIBN | 95 | 56 200 | 1.12 |
| MMA[176] | 34 | BPO | 78 | 47 100 | 1.04 |
| AA[176] | 35 | AIBN | 18 | 13 800 | 1.23 |
| BA[176] | 36 | AIBN | 40 | 92 700 | 1.14 |
| $StySO_3Na$[176] | 37 | ACP | 73 | 8 000 | 1.13 |
| MMA[176] | 38 | AIBN | 92 | 55 300 | 1.05 |
| MMA[177] | 39 | AIBN | >95 | 51 500 | 1.19 |
| MA[177] | 40 | AIBN | 74 | 8 800 | 1.17 |

[a] AIBN = azobisisobutyronitrile, BPO = benzoyl peroxide, ACP = 4,4′-azobis(4-cyanopentanoic acid), MMA = methyl methacrylate, BA = butyl acrylate, AA = acrylic acid, $StySO_3Na$ = p-styrenesulfonic acid sodium salt, MA = methyl acrylate.

Examples of dithioesters (**33**−**40**) successful in mediating RAFT polymerizations are provided below. The key to the degenerative chain transfer step in RAFT is to use dithioesters with extremely high chain transfer constants. This requires Z groups, such as aromatic moieties, that make the C=S group more susceptible to radical addition and R functionalities which are good radical leaving groups (benzyl, cyanoisopropyl).[176] Table 6 provides molecular weight data for a variety of RAFT polymerizations, demonstrating the wide range of vinyl monomers which are polymerizable with relatively low molecular weight distributions (PDI < 1.2).

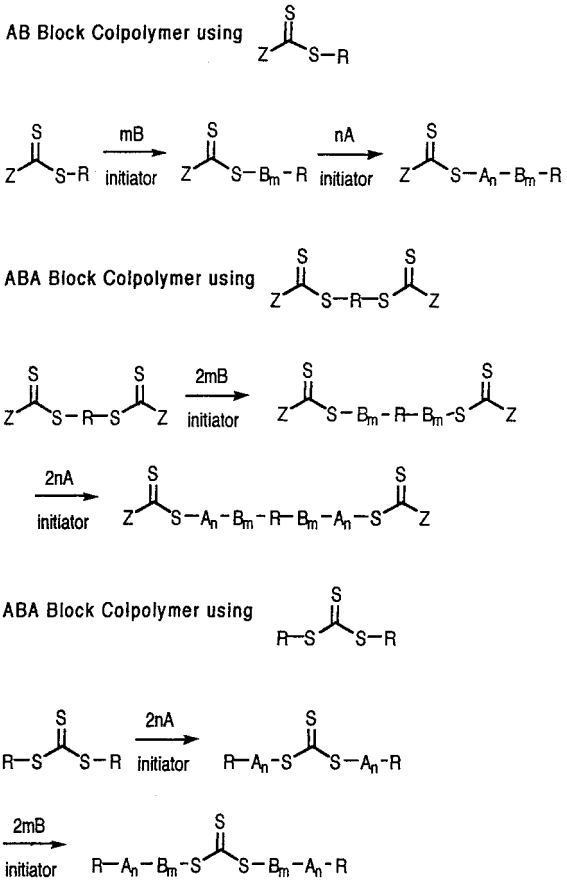


**33**

| | Z | R |
|---|---|---|
| **34** | Ph | $C(CH_3)_2Ph$ |
| **35** | Ph | $CH(CH_3)Ph$ |
| **36** | Ph | $CH_2Ph$ |
| **37** | Ph | $C(CH_3)(CN)CH_2CH_2CO_2Na$ |
| **38** | Ph | $C(CH_3)(CN)CH_2CH_2CH_2OH$ |
| **39** |  | $C(CH_3)_2CN$ |
| **40** |  | $CH_2Ph$ |

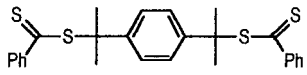
According to $^1H$ NMR of PMA and PMMA samples, the structure of final products synthesized by RAFT

**Scheme 23. Methodology for Synthesizing AB and ABA Block Copolymers with RAFT Mediated by Dithioesters and Trithiocarbonates**

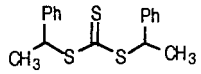



techniques is one where the polymer is end capped with both the dithioester and R moieties, S=C(Z)S−$P_m$−R.[176,177] This structure allows further polymerizations with other vinyl monomers to create various block copolymer architectures. Different AB and ABA block copolymers have been synthesized using multiple-step polymerizations. Scheme 23 shows the general strategy used when conducting RAFT-mediated block copolymerizations using different dithioesters[178] and trithiocarbonates.[179] The addition of initiator is required for *each* polymerization step, resulting in a source of homopolymer impurity when synthesizing the secondary block sequences. It is claimed that the homopolymer impurity can be minimized under the appropriate conditions;[178] this issue will be elaborated on in a later section. AB block copolymerization mediated by **36** yielded styrene and *N*,*N*-dimethylacrylamide blocks with $\bar{M}_n$ of 20 300 (PDI = 1.15) and 43 000 (PDI = 1.24), respectively. Methyl methacrylate (MMA) and hydroxyethyl methacrylate (HEMA) were polymerized into ABA blocks with **41**, where polyMMA (B) and polyHEMA (A) exhibited $\bar{M}_n$ of 23 000 (PDI = 1.16) and 28 500 (PDI = 1.18), respectively.[178] RAFT block polymerizations with trithiocarbonate **42** provided ABA blocks of polystyrene (A) and poly(*n*-butyl acrylate) (B) with $\bar{M}_n$ of 20 100 (PDI = 1.11) and 141 400 (PDI ≈ 1.15), respectively.[179]

RAFT polymerization techniques offer another means of synthesizing vinyl polymers with a well-controlled mechanism. Mediation with dithioesters



41



42

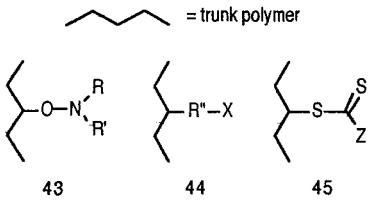
and trithiocarbonates exhibits high versatility in regard to the different types of monomers which are polymerizable, yielding products with low PDIs (<1.20).

## E. Assessment of Controlled/"Living" Radical Methods

Tremendous progress has been made in controlling free radical polymerizations with a "living" mechanism to yield polymers with narrow molecular weight distributions. The utilization of these systems for radical-based graft copolymerization offers many advantages. With strategic placement of the appropriate sites along the trunk polymer backbone, specific macroradical formation can be obtained. Once the polymer chain begins to grow, it can propagate in a more controlled manner to minimize the amount of chain transfer from growing chain ends (provided the monomer-to-initiator ratio is low enough). Both of these features will help minimize homopolymerization. Another major benefit of using a "living" mechanism is that with a narrow dispersity of grafted chain lengths, more uniform properties will result and developing an understanding of structure−property relationships will be more systematic.

Otsu et al. described the conditions for conducting a living radical polymerization mediated by the reversible homolytic scission of a covalent bond that unites the chain end **A** with a labile group **B**. The balance of active and dormant chains requires the formation of "propagating polymer chain ends which may dissociate into a polymer **A** with a radical chain end and small radicals **B**, which must be stable enough not to initiate a new polymer chain".[121] Iniferters that dissociate into different radical species where one is much more reactive than the other in regard to initiating a polymer chain, such as phenylazotriphenylmethane (Scheme 18A), typically have better control over polymerizations relative to iniferters that generate identical radical species, for example, tetralkyl thiuram disulfide (Scheme 17). Although iniferters are an improvement in comparison to conventional means, their "living" nature and control over molecular weight distributions are inferior to those of nitroxides, ATRP, and RAFT.

The utilization of these latter methods for a controlled graft copolymerization would begin with the basic trunk polymer sites shown in **43**, **44** (R″−X is an active halogenated site), and **45** corresponding to nitroxide, ATRP, and RAFT techniques, respectively. Using structures **43** and **44** as the sites for specific macroradical formation, the graft copolymerization would generally proceed in the controlled manner outlined in Schemes 20 and 21 for each respective technique. Controlling a graft copolymerization with

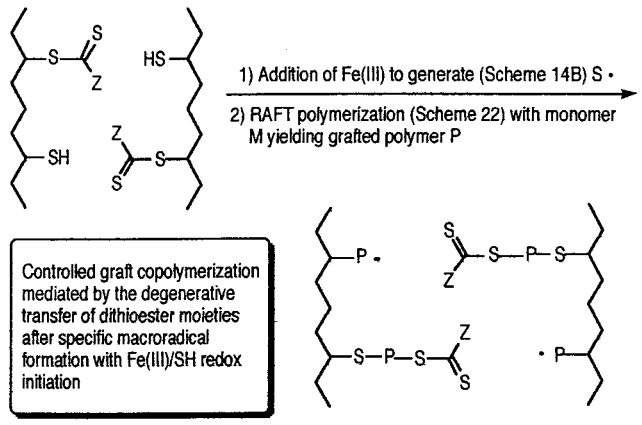



43 44 45

RAFT poses a potential problem in regard to homopolymer formation. Typically RAFT is initiated with the addition of reagents such as AIBN. Utilizing **45**, the addition of AIBN would create radicals in solution to begin the growth of homopolymer. This homopolymer would then react with the dithioester moieties to generate macroradicals. Once the equilibrium of active and dormant chains is established, three types of degenerative transfer could be envisioned, namely, homopolymer/homopolymer, graft/homopolymer, and graft/graft, resulting in complications in regard to homopolymer minimization.

This homopolymer impurity is an issue that has been addressed with previous RAFT block copolymer syntheses. It has been claimed that "it is usually not difficult to achieve block copolymers with no detectable homopolymer impurity (<5%) while still achieving an acceptable rate of polymerization".[178] This claim appears to be promising in the context of this article; however, there are alternative strategies to be considered. For instance, a trunk polymer with dithioester sites along its backbone (**45**) is treated with a nucleophile to convert a portion of these groups to mercapto moieties. As outlined in Scheme 24, the addition of Fe(III) could specifically generate

**Scheme 24. General Approach for a Controlled Radical Graft Copolymerization Combining Fe(III)/SH Initiation with RAFT Mediation**




macroradicals which initiate the RAFT polymerization where ideally only grafted chains participate in the degenerative chain transfer. Most likely being more successful in a homogeneous graft copolymerization, Scheme 24 would promote a more controlled grafting without purposely generating homopolymer to initiate the process.

The likelihood of chain transfer increases with longer kinetic chain lengths with all of these "living" techniques operating under free radical conditions. Thus, it is understood that to truly minimize homopolymerization, the synthesis of lower molecular weight grafted chains would be more beneficial. However, this would not maximize the generation of more uniform chain lengths since increases in molecular weight would promote more narrow molecular weight dispersites (eq 27). Of course, these issues need to be evaluated in order to determine the optimal conditions to conduct the graft copolymerization.

## VIII. Concluding Remarks

Graft copolymer synthesis is important to the development of polymer science with potential uses in areas such as composites, medical applications, fiber modifications, etc. As with any synthesis, product characterization is vital in developing structure−property relationships. Radical polymerizations, being a useful method for the polymerization of a wide variety of vinyl monomers, have classically been plagued by a lack of control over the mechanism; radical polymerizations have many different reactions occurring simultaneously, namely, initiation, propagation, termination by coupling or disproportionation, and chain transfer. Extending the versatility of radical polymerizations, radical graft copolymerizations have been successful in terms of obtaining a grafted derivative; however, grafted product characterization, being inherently difficult in its own right, is further complicated by homopolymer formation. Therefore, major efforts to reduce homopolymer formation have been attempted; however, it is still often amply generated.

The two major sources of homopolymer in radical grafting are nonspecific macroradical formation and chain transfer of growing grafted chains. Several examples of redox-initiating methods have been provided in this article which are effective for specific radical formation; however, chain transfer and molecular weight cannot truly be controlled with these systems. Once the radicals are generated, the mechanism is identical to that of conventional free radical polymerization.

Further reductions in homopolymer generation could be possible when using the more controlled/"living" radical polymerization systems. Although these controlled systems are not perfectly living, under the proper conditions, they do have many of the characteristics of living polymerizations, namely, generation of low PDIs and molecular weights that increase linearly with conversion. Macroradical generation could be feasible with all of the controlled systems described. After the grafted chain begins its growth, the controlling nature of these systems could contribute to further reductions in homopolymer formation. Since these systems are able to generate low PDIs, excellent control over the general polymer architecture would be possible, making the subsequent development of structure−property relationships a more straightforward process.

Certain situations could arise in designing a graft synthesis where creating the necessary site on the trunk polymer to utilize a controlled/"living" system is difficult. In fact, specific macroradical generation could very easily be performed with one of the redox systems discussed previously. For example, the trunk polymer might already have a $CH_2OH$ present on the

backbone such that redox initiation with Mn(III) would be more convenient. An interesting area of research that would combine both systems would be the following: specific macroradical generation could be conducted using the redox-initiating systems followed by the addition of TEMPO or the copper(II)/ligand complex (reverse ATRP) in order to control the growth of the polymer chain. Of course, compatibility issues of the particular systems used would have to be addressed on a case by case basis. For example, combining reverse ATRP with another transition-metal-based system could cause complications because many metal species can undergo metal−metal redox reactions with other metal species, which definitely would interfere with the desired radical generation and subsequent mediation of the polymerization. Combining the nitroxide and RAFT chemistry with the redox initiators could be more successful; however, as mentioned, each particular combination would have to be investigated.

Generally several advances in polymer synthetic chemistry have been made that offer more control over radical polymerizations than ever imagined. This achievement is important not only to grafting synthesis, but also to the creation of other macromolecular architectures, namely, block, star, hyperbranched, etc. In regard to radical graft copolymerization, the controlled radical polymerization systems, possibly in combination with redox initiation, are the best known systems to be considered for grafting trunk polymers with vinyl monomers in hopes of greatly reducing homopolymerization while also having more control over the grafted chain architecture. However, this is not to say that homopolymer will not be formed. Whenever these systems are applied, experimental conditions should be altered to evaluate the performance of these systems in regard to controlling not only the grafted chain architecture, but also the homopolymer yield.

Another important issue with these controlled systems is their compatibility with the trunk polymer to be grafted. In the context of this review, chitin and chitosan offer interesting challenges in regard to these novel initiators. For instance, chitin and chitosan are capable of metal chelation[27] and thus the use of ATRP systems for a chitin/chitosan graft copolymerization will require careful evaluation of how the metal complexes interact with the trunk polymer backbone. However, these types of compatibility issues need to be addressed regardless of the trunk polymer to be grafted. Hopefully further understanding of the chemistries described will be obtained in order to maximize the benefits these systems have to offer toward various types of macromolecular syntheses.

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